

THE TREATMENT OF PNEUMONIA WITH  
2 SULPHANILYL AMINO PYRIDINE

being

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## INTRODUCTION.

Pneumonia has long held a place in the forefront of fatal diseases. . Despite the many investigations which have been carried out regarding its etiology and pathology, the therapeutic problem has remained one of pressing importance. The absence of any definite specific form of treatment has made pneumonia one of that long list of conditions in which the doctor could do little more than deal with the symptoms as they arose. In such a state of affairs, then, there was more than a grain of truth in the well known statement that the successful outcome of a case of pneumonia depended in no small measure on the nursing.

The first advances against the stronghold of pneumonia followed upon the discovery of Docher and Gillespie<sup>1</sup>, who were able to show that the pneumococcus could be classified into Types I, II, III and Group IV. This important information led to the preparation of pneumococcal antisera which were used in the treatment of the disease. A certain amount of benefit was found to result in infections due to Types I and II pneumococcus, but this was dependent



upon the administration of the serum at a very early stage. A further step was made when Cooper et al<sup>2</sup> showed that the heterogeneous Group IV consisted of at least twenty-nine varieties of pneumococcus which they named Type IV to XXXII. Later Dowling and Abernethy<sup>3</sup> reported that antisera were effective against Types V, VII and VIII. Treatment by serum, however, had several important disadvantages. In the first place favourable results were dependent on its early administration. Secondly, it was necessary to know with what type of pneumococcus one was dealing, an insuperable difficulty in any but well equipped hospitals. Thirdly, serum could be administered only in hospital in the majority of cases, and fourthly, a point of no little importance, the cost was considerable. It could not then be said that the problem of the treatment of pneumonia had been solved by the advent of serum and the quest for some universally applicable therapeutic measure had to continue.

Since the time of Ehrlich's discovery of the effect of the mercurial drugs on spirochaetal infections, advances of great importance have been made in the therapeutic control of the higher forms of micro-organisms. No substance, however, had been found

which would act effectively in vivo on the lower grade bacteria. It was at this stage then that in 1935 Domagk<sup>4</sup> and his associates Meitzsch and Klarer found that an azo-dye containing a sulphanamide group was effective in the treatment of streptococcal infections. This preparation was known as Prontosil. Shortly after its discovery it was found that the active properties of the drug lay in the colourless part and the original prontosil became replaced by that portion known as Sulphanilamide. This treatment of streptococcal infections by Sulphanilamide, so simple in use and so universally applicable, opened up a field of tremendous possibilities and it was natural that, almost immediately, the effect of this drug in diseases caused by other organisms should be investigated. That an enquiry into its effectiveness on pneumococcal infections was carried out at an early date is in no way surprising.

Originally Domagk gave the impression that Sulphanilamide had some action on Type III pneumococcus, but none on Types I and II. Later, Nitti Bovet and Depierre<sup>5</sup> found that, in vitro, sulphanilamide had an inhibitory effect on the pneumococcus, while Britton<sup>6</sup> noted a definite but variable bacteriostatic and

bactericidal effect on Types I and II and on Group IV pneumococcus. Whitby<sup>6</sup>, however, found almost no protection given by sulphanilamide against 10,000 lethal doses of Type I pneumococcus. On the whole, then, the effect of sulphanilamide on the pneumococcus was variable and the final impression was that results did not seem to justify its use in the treatment of Pneumonia.

Fortunately, however, this failure of Domagk's sulphanilamide in its action against the pneumococcus did not end the story. His discovery had given a new stimulus to the treatment of disease by chemotherapeutic measures and almost immediately a large number of compounds allied to sulphanilamide were prepared by the research chemists. Several of these substances were found to be more active than sulphanilamide against the pneumococcus but had the disadvantage of being relatively toxic. Thus Buttle<sup>7</sup> found that the benzylidene Schiff's base of diamino-diphenylsulphone was more effective than sulphanilamide in prolonging the life of mice infected with Type I pneumococcus and that half the mice infected with one lethal dose survived for thirty days. This preparation, however, was four times as toxic as



sulphanilamide. Similarly, Whitby<sup>8</sup> found the diamino benzene sulphanilamide compounds about three times more efficient than sulphanilamide for Type I infections in mice. After comparative examinations of a large number of compounds, the preparation 2-sulphanyl-aminopyridine was selected for further investigation. This product was first prepared in the chemical laboratories of May and Baker, Ltd., in England, and has been given the popular name of M. & B. 693.

The experimental trials of M. & B. 693 were carried out by Whitby<sup>9</sup>, using mice infected with the pneumococcus. He found that the drug gave protection against pneumococci of Types I, II, III, V, VII and VIII. He also concluded that for the experimental animal the drug had a low toxicity. Support for Whitby's finding was forthcoming from the results of in vitro experiments carried out by Fleming<sup>10</sup>.

Following upon the experimental evidence of Whitby and Fleming, the next step was to administer M. & B. 693 to man and to observe its effect on human pneumococcal infection. In July 1938 Evans and Gaisford<sup>11</sup> published a report on two hundred cases of lobar pneumonia, half of which were treated with M. & B. 693.



In those treated with the drug the mortality was 8 per cent., while in the control series it was 27 per cent.

The possibility then, that a preparation had been discovered which would give effective results in the treatment of pneumococcal infections in man was something of no little interest to all concerned in medicine. At this stage M. & B. 693 was becoming available for trial and I therefore determined, if it were at all possible, to observe its effects for myself.

After qualifying in 1936 and having spent eighteen months in hospital and six months in general practice, in October 1938 I became resident house physician to Dr W. A. Alexander in the Royal Infirmary, Edinburgh. Through his kindness and that of other members of the honorary staff, I was enabled to visit all the cases of pneumonia admitted under six of the medical charges and to follow their treatment with M. & B. 693.

In carrying out any investigations as a house physician, there are of necessity certain limitations in view of the pressure of routine duties and the work of running medical wards. Under the circumstances,

then, it seemed that the observations which could be made with the greatest care and success would undoubtedly be those of a clinical nature. Having thus pondered and realised my limitations as regards any investigation I might make into the treatment of pneumonia with M. & B. 693, the question then arose as to what light, if any, might be thrown on the matter by such an enquiry.

At first the consideration of this question filled me with despair, for as a resident in hospital one is surrounded by well equipped clinical laboratories. In consequence one is apt to feel that no investigation is complete which does not employ some of the many tests that may be carried out there. I knew that I had neither the time at my disposal nor the necessary aptitude to carry out these clinical laboratory investigations of the effect of M. & B. 693 on pneumonia. Some consideration, however, led me to conclude that an investigation from a mainly clinical standpoint might give information of no small usefulness, and indeed the more I thought of it the greater seemed its importance.

The reports of the first trial of the drug M. & B. 693 (Evans & Gaisford<sup>11</sup>) in human beings suffering

from pneumonia had shown that in the majority of cases certain dramatic results had been obtained - results which, if they were substantiated by further observations, indicated that the course and ultimate outcome of pneumonia were going to be greatly changed. If then I could treat a reasonable number of cases with M. & B. 693 and observe from the clinical standpoint the result of such treatment, an opinion could be formed as to its efficiency or otherwise. In the event of such observations justifying the conclusion that the drug influenced the course of pneumonia favourably, certain other important questions must then be answered.

It is well known that a drug which can be used in hospital where every facility is available for its administration and control cannot always be employed with ease in other surroundings, particularly those met with in general practice. M. & B. 693, then, might prove itself of great service in the treatment of pneumonia, but its use with safety might entail elaborate investigations, for example regarding its concentration in the blood stream, its rate of excretion by the various routes, and so on. Should such prove to be the case, then the scope of the drug



would be greatly reduced from the outset. If on the other hand it was found that an adequate concentration could be attained and maintained in the blood after a stated dosage, that such dosage produced the expected result and gave the necessary margin of safety, then useful information had been gained regarding this drug M. & B. 693.

The next step, having been satisfied as to its effectiveness, safety and reasonable facility of use, was to enquire into the question of how extensively it might be employed against the pneumococcus. The pneumococcus which is most often the causal organism of pneumonia has now been differentiated into thirty two types, each showing agglutination to specific sera (Dochez and Gillespie<sup>1</sup> at Rockefeller Institute, New York, and Cooper, Rosenstein, Walter and Peizer<sup>2</sup>).

It was now necessary to reach a conclusion as to whether or not M. & B. 693 had a useful effect in pneumonia, as it affects human beings, due to any one of these thirty two types of pneumococcus occurring singly or as a mixed infection. Was it more effective against one type of pneumococcus than another, or the same in its action against all? The efficacy of the drug in pneumonia due to organisms other than the



pneumococcus, e.g. the streptococcus, was also of the utmost importance. In fact it would be necessary to form an opinion as to whether, should a case be diagnosed clinically as pneumonia, the administration of M. & B. 693 could be depended upon to give uniform results in the majority of cases. This latter question is one of outstanding importance on consideration of the fact that facilities for determining the type of the infecting organism are not always available.

An answer having been given to the foregoing questions - should M. & B. 693 have been shown to be satisfactory in these respects - it still remained to be seen whether or not this drug presented any advantages over other forms of treatment already in use. To reach a conclusion on this point in a clinical investigation it would be necessary to consider certain factors. The first of those factors would be the effect of the drug on the mortality from pneumonia. It has long been known that the severity of pneumococcal infections varied from year to year (Painton and Ulrich<sup>12</sup>) and consequently the mortality has also been variable. At the same time the death rate has never been in any sense a low one. Thus cases admitted to the Royal Infirmary, Edinburgh, show the

following mortality figures for all cases of pneumonia.-

1933-34	..	..	23.28%
1934-35	..	..	28.4%
1935-36	..	..	41.66%
1936-37	..	..	40.2%
1937-38	..	..	30.22%.

The mortality also varies in the different Types of infection. In Type I infection, then, the Medical Research Council's<sup>13</sup> mortality figure was 15 per cent. and that of Cruikshank<sup>14</sup> from a series of cases in Glasgow 10.8 per cent. Cecil<sup>15</sup> in America, from a large number of cases, reported a mortality of 28.8 per cent. In Type II infections these three authorities publish mortality figures which are slightly higher than for Type I, viz., Medical Research Council 27 per cent., Cruikshank 21 per cent. and Cecil 48.8 per cent. With regard to Type III there is general agreement that this organism is prone to attack people over 40 years of age and in them is peculiarly fatal. It has generally been thought that the mortality from Group IV infections was lower than from other forms. Thus Cruikshank reported 8.6 per cent. and Davies, Hodgson and Whitby<sup>16</sup> 7 per cent. These figures are in striking contrast to that of 31 per cent. quoted by Cecil.

If, then, a significant alteration in these figures could be shown to occur in cases treated with M. & B. 693, information of the greatest importance regarding the drug would have been obtained.

Further, by clinical observation the effect of the drug on the course of pneumonia could be observed. Regarding the effect of M. & B. 693 on the course of the disease, three important questions presented themselves for answer. Firstly, what effect did the drug have on the course of the severe stage of the illness - that period during which the patient has a high temperature, greatly increased respiratory rate, is very toxic and often gravely ill? Could it be shown that M. & B. 693 in any way influenced this most anxious period of the disease - was this period in any way shortened or made less severe? Secondly, was the period of convalescence influenced in any way? Was the patient able to get out of bed sooner? Thirdly, was he able to return to his work at an earlier date than after other forms of treatment?

In this connection the question of the time taken for the inflammatory process in the lungs to resolve was of importance. In a typical case of lobar pneumonia all signs in the lung have usually disappeared



fourteen days after the onset of the disease (Price, F. W.<sup>17</sup>). Was then this period of resolution shortened or was the action of M. & B. 693 such that some delay occurred in this stage of the illness?

Perhaps the most common serious complication of pneumonia is the occurrence of empyema and consequently one point of great interest in this clinical study of pneumonia treated with M. & B. 693 would be its effect on the occurrence of empyema. What then was the incidence of empyema in cases of pneumonia treated with M. & B. 693? Could it be said that fewer or more cases occurred with this form of treatment than before its inception?

One of the most important factors which determines the suitability for use in human beings of any drug is the presence, and should it exist, the degree of its toxicity. Vital information concerning this very important point is certainly obtained by observation of effects of administration of the drug to animals. The final test, however, taking guidance from the results of animal experiments, must be the giving of the drug to a human subject, the while carefully watching all the ways in which toxicity may show itself. Thus in my clinical study it would be



necessary to be continually watchful for signs of severe toxic symptoms - signs which might indicate that the effects of the drug were of themselves as dangerous as the disease. The occurrence of symptoms of this nature would immediately indicate the unsuitability of the drug for use in disease in the human subject. At the same time it would be necessary to distinguish from these toxic symptoms those phenomena which, while they might be regarded as due to the use of the drug, would be of insignificant import and constitute only an inconvenience and not a danger or contraindication to its use. In the event of the appearance of these relatively harmless manifestations, could anything be done to overcome or circumvent them?

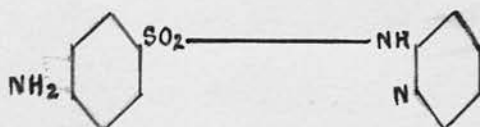
Having treated a number of cases with M. & B. 693 it should be possible to form some opinion as to the cost of the amount of the drug necessary to bring about the desired effect. Could it be said that this form of treatment was within the reach of everyone's pocket?

From a clinical investigation it should, then, be possible to reach conclusions on these various points. These conclusions having been drawn, it should then be possible to answer a final question. Could the drug

M. & B. 693 be used with safety and reasonable certainty of good results by the general practitioner of medicine? For only when a drug can be used by all members of the profession, no matter the conditions under which they work, can it be said to be in the highest degree useful.

THE ACTION OF M. & B. 693.

The drug now known in this country as M. & B. 693 is related to both Sulphanilic acid and Amino-pyridine as is shown by the structural formula



In earlier publications it was referred to as 2- p-aminobenzenene-sulphanilamide pyridine, but is now referred to as 2- sulphanilyl-aminopyridine. Because the drug is universally known as M. & B. 693 and for simplicity I shall refer to it by this name throughout.

Properties of M. & B. 693.

M. & B. 693 is a white or nearly white crystalline powder melting at 190-193°C. and having a slightly bitter taste. It is soluble in water to the extent of about 1 in 1000 and it is sparingly soluble in the usual organic solvents. M. & B. 693 possesses acid and basic properties. It is the free amino group which confers the basic properties while the acidic properties depend on the sulphonamide hydrogen.

Fate of M. & B. 693 in the Body.

Despite its sparing solubility in water (1 in 1000) M. & B. 693 has been shown to be rapidly absorbed from the gastro-intestinal tract in animals (mice, rabbits and dogs), and in the human subject. (Baines and Wien<sup>18</sup>.) These investigators have found measureable quantities of the drug in the blood stream within one hour of ingestion. As with sulphanilamide, M. & B. 693 is detoxicated by acetylation in both rabbits and human beings (Stokinger<sup>19</sup>). Feinstone and Long<sup>20</sup> find that the acetylated form of the drug has little or no chemo-therapeutic effect. In rabbits, Baines and Wien<sup>18</sup> found that the administration of a dose of 0.5 mgm. per gm. M. & B. 693 a concentration of 1 in 10,000 was reached and in mice doses above 5 mgm. resulted in a blood level of 1 in 3,000. In rabbits they found that after giving 0.5 mgm. per gm. of the drug by stomach tube, the concentration of M. & B. 693 in the blood stream reached its maximum at the end of the second hour with the value of 11 mgm. per 100 c. cm. After five hours the concentration had dropped to half this level and at the end of twenty-four hours the drug was completely absent from the blood stream. The free amino body was present in a concentration of 75 per cent., while the conjugated form reached the



level of 25 per cent. Further determinations showed that all the free amino body was present in the serum. This latter observation is in accordance with the findings of Fleming<sup>10</sup>, who found the activity against pneumococci rested in the serum of patients treated with the drug.

In man, Baines and Wien<sup>18</sup> found that single doses of 1 gm. and 2 gm. gave concentrations in the blood of 1 in 50,000 and 1 in 25,000. Further, they observed that following a single dose of 1 gm. M. & B. 693 the drug appeared in the blood after one hour, reached its maximum in from five to seven hours, falling thereafter and being completely excreted in fifty hours.

In experimental administration of the drug to a patient, Hobson and McQuaide<sup>21</sup> found that 1 gm. given at two hourly intervals produced a concentration in the blood of 1 in 10,000.

Long and Feinstone's<sup>20</sup> results showed that a dose of 0.05 gm. per gm. to a man produced a maximum blood concentration of 3.2 to 5.6 mgm. per 100 c. cm. in four hours and that almost all the drug was present as the free amino body.

That M. & B. 693 can penetrate to other tissue fluids is shown by the observations of Hobson and McQuaide<sup>21</sup> who found the drug in the cerebro-spinal

fluid in concentrations of approximately fifty per cent of that in the blood. Its presence has also been demonstrated in purulent pleural exudates by Long and Feinstone<sup>22</sup>, who found there a concentration of half to two thirds that in the blood.

Variations in the concentration of the drug in the blood stream were shown to occur by Hobson and McQuaide<sup>21</sup>. In a patient suffering from meningococcal meningitis treated by them with M. & B. 693, the maximum concentration reached in the blood stream was 4 to 6 mgm. per 100 c. cm., while in a trial administration after the patient's recovery the maximum concentration was between 8 and 10 mgm. per 100 c.cm. They concluded from their work that the concentration of M. & B. 693 in the blood stream might vary with the state of the patient's health, the state of alimentary tract and probably with the fluid intake of the patient. Stokinger<sup>19</sup> found that where there was a high level of acetylation the concentration of the free form in the blood was low, and states that the wide variation of the drug in different cases might depend on three possible factors, viz. rate of absorption, rate of acetylation and rate of elimination of free and acetylated forms. In general he found that cases on a higher dosage tended to have a higher blood

concentration. This latter observation is borne out by Graham et al.<sup>28</sup>

Excretion of M. & B. 693.

The experiments of Baines and Wein<sup>18</sup> lead them to believe that the drug is excreted almost entirely in the urine, there being only a very small percentage present in the faeces. They found the drug in the urine about one hour after ingestion, one half as the free amino body and the remainder as the acetyl compound. Excretion was found to be complete fifty hours after the administration of 1 gm. to a man. Long and Feinstone<sup>20</sup>, giving 0.05 gm. to a man at six hourly intervals for one day, found that 65 per cent. of the drug was excreted in three days and that amounts varying between 30 and 70 per cent. were present as the free amino body. Stokinger<sup>18</sup> recovered 1.82 and 2.4 gm. of the acetyl derivative of M. & B. 693 in two twenty four hour specimens of urine from a patient who had received 9.5 gm. of the drug over a three day period; no free drug in the urine after 24 hours; acetylated form absent 48 hours. He also found crystals of the acetyl compound depositing spontaneously in the urine of rabbits and men.



Mode of Action of M. & B. 693.

Whitby<sup>9</sup> was among the first to publish evidence of the activity of this drug using the pneumococcus as the test organism. He found that six doses of 30 to 40 mgm. of M. & B. 693 gave complete protection to mice inoculated with 10,000 lethal doses of Type I pneumococcus and that in doses of 20 to 40 mgm. there was complete protection against Types VII and VIII. In Types II, III and V, protection was not complete but was high. In the experiments on Type I pneumococcal infection observations were carried out on forty-two mice for a period of fourteen days after the conclusion of treatment and no late deaths occurred. Thirty mice were reinoculated at the end of the first week with another 10,000 lethal doses and were found to be immune to this second infection.

Following upon the publication of the above findings, investigations were carried out in an endeavour to elucidate the mode of action of the drug on the Pneumococcus.

Fleming's<sup>10,23</sup> in vitro experiments led him to conclude that M. & B. 693 had a powerful bacteriostatic effect in de-leucocytized blood and that when it was present in normal blood in 'suitable' concentrations there was increased destruction of pneumococci.

Leucocytes were necessary for this destruction. In a later communication he states that the anti-bacterial power lies in the serum, and that the efficiency of the leucocytes is not increased. He further concludes that M. & B. 693 added to human blood or contained in the blood of patients taking the drug does not prevent encapsulation of pneumococci.

McIntosh and Whitby<sup>24</sup> carried out experiments dealing with the effect of the drug on the specific and non-specific body defences and with its action on the bacteria. Their findings support the view that M. & B. 693 has no stimulating effect on the leucocytes, phagocytic cells or the specific immune defences of the body. They go further and say that since an in vitro effect can be demonstrated in serum or broth as well as in whole blood, it would not seem that leucocytes are a primary requirement.

Several interesting features were brought to notice regarding the action of the drug on the bacteria. It was demonstrated that in the presence of M. & B. 693 the bacteria multiplied for about four hours and it was not till after this interval that any counter effect was seen. Further, the drug was observed to be inactive against rough or avirulent cultures. The explanation advanced by the authors to explain these

findings is that M. & B. 693 in some way interferes with the essential food supply of the organisms. The fact that the drug is inactive against rough and avirulent organisms, they say, tends to support this view in that the food demand of these organisms is not so exacting.

A further effect observed in their experiments was the phenomenon of capsular degeneration, found in vivo and only in peritoneal samples. This capsular degeneration has also been observed by Telling and Oliver<sup>25</sup> in the sputum of a patient suffering from a Type III pneumococcal infection. Using Gram's stain they examined a specimen of the patient's sputum after the administration of 3 gms. M. & B. 693. The organisms were found to be scanty, pleomorphic and non-capsulated. Primary culture yielded a pure atypical growth, not agglutinated by Type III or any other serum. Mouse inoculation yielded an exudate which on culture showed the same pure atypical growth and no agglutination by any serum. Passage of this strain restored its previous characteristics.

In experimental work, Hilles and Schmidt<sup>26</sup> found decapsulation of pneumococci from peritoneal fluid after death. They proved that these decapsulated organisms were avirulent.



Experimental evidence regarding the concentration of the drug necessary to be effective against the pneumococcus has been furnished by McIntosh and Whitby<sup>24</sup>. Using 2 c.cm. citrated rabbit's blood they found that the limit of activity of M. & B. 693 in a concentration of 16 mgm. per 100 c. cm. was somewhere between 50,000 and 150,000 pneumococci: 8 mgm. per 100 c.cm. was effective against 150, 4 mgm. against 2, and that concentrations of 2 mgm. per 100 c.cm. were ineffective against the smallest inoculum.

In the human subject, Flippin et al<sup>27</sup> examined the blood level in two series of cases treated with M. & B. 693. The end results in eleven patients showing a blood concentration of 1 to 2.8 mgm. per 100 c. cm. were compared with those of eleven patients showing a blood concentration of 10 to 18 mgm. per 100 c. cm. Nine of the patients in the former group showed a fall in the temperature in the first twenty-four hours, while only six in the latter showed a fall of temperature in the first twenty-four hours. From these findings they concluded that a concentration of 10 mgm. per 100 c.cm. or more, was unnecessary and produced no greater effect than a concentration of 1 to 2.8 mgm. per 100 c.cm.

Graham et al<sup>28</sup> found that a concentration of

10 mgm. per 100 c.cm. was the exception rather than the rule even with dosages as high as 12 gm. in the first day of treatment and 9 gm. on the second. With this dosage they found concentrations varying from 2.3 mgm. per 100 c.cm. to 17 mgm. per 100 c.cm., the majority being in the region of 7 to 8 mgm. per 100 c.cm. which was effective.

In this series of cases I have not carried out any estimations of the concentration of the drug in the blood stream as the endeavour has been to keep the survey completely along clinical lines. It has been found that a dosage varying in the average from 6.5 gms. to 8.5 gms. given in the first thirty-six hours is sufficient to give an adequate concentration in the blood as judged by the effect on the temperature, pulse and respirations and general condition of the patient. If a dosage of this size was spread out over a longer period in its administration, the time taken for general improvement in the patient's condition was correspondingly longer. This fact may be exemplified in case K<sub>2</sub>, in which a dosage of 7 gms. was given over a period of seventy-two hours with a fall of temperature, etc., after this time. Similarly in case L<sub>4</sub>, where 7 gms. was given in a period of thirty-two hours. It therefore seems probable

that in the majority of cases which are going to respond to M. & B. 693 a dosage of 6.5 to 8.5 gms. should be given within a reasonably short period of time, possibly within the first twenty-four hours.

#### Toxic Effects of M. & B. 693.

The toxicity of M. & B. 693 for animals was investigated by Wien<sup>29</sup>. The daily administration of 0.5 mgm. per gm. to rats for two weeks had no effect on the blood or urine, and similarly, doses of 1 gm. daily for seven days to dogs and cats had no effect on the blood, urine or general health. M. & B. 693 given in two and four times the dose of sulphanilamide caused no increase in excretion of urinary porphyrin or decrease in the red cell count. Toxic symptoms, however, have been recorded in man, the most common being nausea, vomiting, headache and malaise (Flippin et al<sup>27</sup>, Lloyd et al<sup>30</sup>, Cunningham<sup>31</sup>, Batchelor<sup>32</sup> and Brown<sup>33</sup>). In the majority of cases these symptoms were not sufficiently severe to interfere with treatment. Batchelor et al<sup>32</sup> found that a reduction in dosage overcame the symptoms. But Graham et al<sup>28</sup> have stated that in the presence of nausea and vomiting continuance of the drug tends to decrease rather than increase the symptoms. Barnett et al<sup>34</sup> are in



agreement with this.

Among methods employed to overcome the above toxic symptoms, Flippin et al<sup>27</sup> have found the following methods of use, viz. the administration of small amounts of soda bicarbonate, crushing the tablets and administering in milk, passing a duodenal tube and administration of the drug through this. These means have also been found effective by Fahrni<sup>35</sup>.

Skin rashes have been present in a small proportion of cases. Batchelor et al<sup>32</sup> observed dermatitis in six out of one hundred and two cases of gonorrhoea treated with the drug, Graham et al<sup>28</sup> in two out of fifty cases of pneumonia, and Fahrni<sup>35</sup> in one out of twelve cases of pneumonia. In all cases the rash disappeared within a short time of discontinuance of the drug.

Hallam<sup>36</sup> has reported a case in which the rash appeared only after exposure to ultra-violet light.

The occurrence of haematuria has been observed in four out of fifty patients by Graham et al<sup>28</sup>, who found jagged crystals of the drug in the urine of these patients.

Though very few cases have been reported, the most serious complication has been agranulocytosis. Graham et al<sup>28</sup> found a white cell count of 900 per

c.mm. in a patient who had had 79 gm. of the drug, but who recovered with stoppage of the drug. Barnett et al<sup>34</sup> recorded a case in which the white blood cells fell to 75 per c.mm. after 80.9 gm. of the drug. The count subsequently rose to 22,500 per c.mm., but the patient died later of haemorrhage from cervical adenitis. On the whole, therefore, it would seem that the toxic effects of M. & B. 693 are mild, are quickly recovered from and produce no lasting effect.

In this series of 82 cases the toxic symptoms have been of little consequence. The only ones observed have been cyanosis and vomiting, both of which have been transient and had no lasting effect. In the majority of cases the treatment has been continued in spite of these symptoms, the tablets being given crushed in milk or with sodium bicarbonate. The white blood count has been observed throughout the cases and no significant fall has been recorded during the administration of the drug or following its cessation.

ETIOLOGY AND PATHOLOGY OF PNEUMONIA.

Pneumonia is an acute inflammation of the lungs due to bacterial invasion, the disease being characterised by fever, toxæmia of varying degree and by evidence of pulmonary consolidation. The disease is one of the commonest phenomena in medical practice and has been sub-divided into several groups.

Thus Burrell<sup>37</sup> classifies pneumonia under the headings of -

- (a) Typical acute pneumonia.
- (b) Broncho-pneumonia following a foreign body in a bronchus.
- (c) Secondary pneumonia - probably a plug of mucus causing collapse.
- (d) Sub-acute and Chronic pneumonia.

ETIOLOGY OF PNEUMONIA.

More recently the importance of the organisms causing the disease has come to the front. Any organism entering the respiratory tract may cause pneumonia, but certain bacteria are more commonly responsible. Thus although the main organism is undoubtedly the pneumococcus, the importance of the Streptococcus, B. Friedlander and the causal organisms of Influenzal Pneumonia cannot be dismissed lightly,



as Gaskell has shown that the outcome as far as the lungs are concerned depends on the type of organism.

Streptococcal pneumonia does not commonly affect healthy adults and appears more often at the extremes of life - in the young and in the aged. When it attacks an adult it is usually when he is in a condition of lowered resistance. The non-haemolytic streptococcus is an organism of low virulence and pneumonia due to it occurs usually as a terminal event, but it may be responsible for a mild form of pneumonia with a low mortality.

The haemolytic streptococcus, on the other hand, produces a widespread pneumonia which is liable to be complicated by abscess formation and empyaema. It is also prevalent as a secondary invader in influenzal pandemics.

The B. Friedlander is fortunately not a common causal agent in pneumonia, as it is peculiarly fatal.

The staphylococcus usually occurs as a secondary invader and is more likely to cause the so-called broncho-pneumonia with abscess formation.

The modern conception of influenzal pneumonia is that it is due to a virus. It would appear that this virus is capable of lowering the resistance to such a degree that the lungs lie open to attack by a secondary

invader. The secondary invader may be the pneumococcus, streptococcus or staphylococcus, but in many cases is the B. Pfeiffer, which is found in large numbers in many cases of this type.

### PNEUMOCOCCAL PNEUMONIA.

#### Bacteriology and Etiology.

The typical appearance of the pneumococcus is that of a lanceolate or oval coccus in pairs, with the rounded ends together. It is about 1  $\mu$ . in its long diameter and shows a thick capsule which appears as an unstained zone round the organism unless positively stained by special methods (Mackie & McCartney<sup>38</sup>). In 1913 Dochez and Gillespie<sup>1</sup>, investigating a series of cases of pneumonia in search of a specific therapy showed that the pneumococcus could be divided into four definite groups, which they designated, Type I, Type II, Type III, and Group IV. Types I, II and III were shown to be sharply defined from each other and from Group IV by their agglutination with specific type antisera.

No further differentiation of the pneumococcus was attempted till 1929, when Cooper et al<sup>2</sup> started to investigate the homogeneous Group IV. Ultimately

these workers were able to show that this group contained at least twenty-nine antigenic types, sharply defined from each other and differentiated by specific agglutination. The possibility that other types of pneumococci do exist is not ruled out, but it seems probable that the types pathogenic to man are all contained in Types I, II, III and the twenty-nine varieties of Group IV, named from Type IV to Type XXXII, (Topley and Wilson<sup>39</sup>).

The capsule of the pneumococcus has been shown to be responsible for the antigenic behaviour of the organism. According to Topley and Wilson<sup>39</sup>, the antigenic structure of the pneumococcus may be as follows: there is a central protoplasmic portion which in its antigenic behaviour is neither species nor type specific. At the cell surface is another component, mainly carbohydrate in nature and containing nitrogen and phosphorus, which is specific for the pneumococcus as a species. Finally, external to those in the normal smooth form is a capsule consisting wholly or in part of a polysaccharide which is specific for each pneumococcal type. There is reason to believe now, that besides being responsible for the antigenic relationship of the organism, the capsule plays an important part in determining the virulence of the

pneumococcus.

That the pneumococcus may be present in the throat and nasal passages of normal individuals has been shown by Webster and Hughes<sup>40</sup>. They found the organism present in eighty per cent. of the normal people investigated by them and in ninety-seven per cent. it was serologically specific. Types I and II were found in one and two people respectively and under circumstances suggesting that these organisms were not able to spread rapidly. Types III and XII were present in nine people each and there was evidence to suggest spread from person to person. Types XVI and XVIII were present in three people. Smillie<sup>41</sup> (1933) showed that Types III to XIX were prevalent in the throats of the general public and that the most frequent types were III, VI and XVIII. Sutliff and Finland<sup>42</sup> found that eighty-four per cent. of their series was composed of Types I, II, VIII, V and VII in that order of frequency. Their investigations have led them to the further conclusion that in ninety-six per cent. of those shown to have Type V pneumococcus in the throat or nasal passages, pneumonia occurred, similarly in ninety per cent. of those with Type VIII and eighty per cent. of those showing Type VII. Generally speaking, then, while Types I and II



are rarely found in the throat or nasal passages of normal people, other types occur with varying frequency. Usually it has been held that the organisms in the so-called Group IV are less virulent and that pneumonia is less likely to result from these organisms. Doubt as to the accuracy of this belief has been evidenced in the experiments of Sutliff and Finland<sup>42</sup>.

#### PATHOLOGY and SPREAD.

In its pathological description pneumonia has been divided into four stages, viz.- stage of engorgement, stage of red hepatization, stage of grey hepatization and resolution. In the stage of engorgement the blood vessels of the alveoli are swollen and engorged and there is an outpouring of fluid containing leucocytes and red blood cells into the alveoli. In the stage of red hepatization the lung is consolidated firm and airless. The overlying pleura has lost its shiny surface and is covered by a thin coat of fibrin. The alveoli are packed with firm clot composed of a meshwork of fibrin in which are entangled pneumococci, red blood cells and polymorphonuclear-leucocytes. When the process proceeds to grey hepatization, the lung becomes dense hard and heavy and its surface is

covered with a thick layer of fibrin. The alveoli are packed with degenerated cells in the shape of leucocytes, a few red blood cells and numerous desquamated cells. When resolution commences, the lung is soft, friable and very translucent, while the contents of the alveoli are more degenerated and less in quantity (McCallum<sup>46</sup>).

In the production of pneumonia the experimental work of Blake and Cecil<sup>43</sup> has been of great importance. Using monkeys they were able to produce lobar pneumonia as it occurred in man. They found that inoculations into the throat and nose or into the blood stream did not produce lobar pneumonia. To do so they showed it was necessary to inoculate the trachea, and that this was the only means of producing the disease. This work, coupled with the knowledge that pneumococci may exist in the throat of healthy people, makes it seem probable that the most usual, if not the only route of infection in man is by way of the trachea and large bronchi.

After infection, Blake and Cecil showed that the initial invasion occurred close to the hilum of the lung. From there their evidence indicates that the infection invaded the lymphatics, peribronchial, perivascular and septal tissue and that the invasion of

the alveoli took place from those interstitial tissues. They further concluded that hepatization was central in origin, spreading thence to the periphery. More recent work has cast doubt on the possibility of this mode of spread and it seems probable that the opinion advanced by others - among them Terrell Robertson and Coggeshall<sup>44</sup> and Gunn and Nungester<sup>45</sup> - is more correct. The view advanced by these observers is that the spread of infection takes place from alveolus to alveolus through Cohn's pores by means of infected oedema fluid.

By means of X-ray, Davies Hodgson and Whitby<sup>16</sup> investigated the spread of the pneumonic process from its earliest stages in a series of patients under their care. They found that changes were first apparent in the hilar region in the form of an increase in the size of the hilar shadow and deepening of its density. From the hilum the opacity spread rapidly to the periphery which, in the majority of cases, was the last region involved. They noted that in the case of infections due to organisms of Type III and Group IV the process occasionally started at the periphery and spread inwards. In all cases spread took place rapidly and was well marked in the X-ray plate within twenty-four hours.

DETERMINATION of PNEUMONIA.

The question of what actually determines the onset of an attack of pneumonia is still open to argument. It seems likely that the virulence of the attacking organism and the resistance of the host must in some way be intimately concerned. The significance too, of the fact shown by Blake and Cecil<sup>43</sup> that to produce pneumonia the organisms must reach the trachea and the observations of Webster and Hughes<sup>40</sup>, and Sutliff and Finland<sup>42</sup>, that the organisms except in the case of Types I and II may be present in healthy individuals, must bear some relationship one to the other.

Stillman<sup>47</sup> found that he could produce pneumonia in mice only when they had recovered from the effects of a previously inhaled spray of pneumococci. In man, Ward found that the blood of early untreated cases of pneumonia had a high capacity for killing pneumococci in vitro. Sutliff and Finland<sup>42</sup> have shown that the blood of normal individuals had the power to kill pneumococci. They further observed that during the first two years of life this power was very small but that it increased with age, reaching its maximum about the age of forty. The pneumococci-cidal power of the blood of a normal individual appears



to bear some relationship to the incidence of pneumonia in various age groups.

The abruptness of onset and rapid spread of the inflammatory process in the lung has suggested that the condition might be an expression of altered sensitiveness of the lung to the pneumococcus. Sharp and Blake<sup>48</sup> in experimental work on rabbits reached the conclusion that the inflammatory process in the lung depended on an allergic state rather than on the inherent injurious substances in their autolysate.

Fried<sup>49</sup>, investigating the allergic theory, injected small amounts of horse serum into the lungs of normal rabbits and showed this to produce a transient inflammation confined to the dorsal aspect. A further injection of horse serum into the sensitised lungs produced lobar pneumonia in a high percentage of cases.

In man it has been shown by various observers (Clough<sup>50</sup>; Steinfeld<sup>51</sup> and Kolmer; Bigelow<sup>52</sup>) that percentages varying between fifty and eighty-five of normal people react locally to an intracutaneous injection of pneumococcus antigen and that during the acute stage of pneumonia the skin is not reactive to these antigens.

SELECTION and TREATMENT of CASES.

A diagnosis of Lobar Pneumonia was established in all the cases of this series on clinical grounds. In many instances confirmation was given by X-ray examination and, where any doubt existed, such an examination was always carried out. In view of the reports of Wein<sup>29</sup> of the low toxicity of the drug, and the support given to this by the findings of Evans and Gaisford<sup>11</sup> in their original series of cases, and because of the favourable results obtained by them, it was decided to make no selection of the cases admitted. All of them were treated with 2 sulphanilyl aminopyridine (M. & B. 693) irrespective of their age or of the stage which the disease had reached.

Immediately on admission, after a history of the illness had been obtained, in which care was taken to establish the day of the illness, a specimen of sputum was secured. This was sent for bacteriological examination with a view to finding the organism present and, should this prove to be a pneumococcus, to what type it belonged.

After the specimen of sputum had been obtained, treatment with M. & B. 693 was instituted. The initial dosage consisted of four tablets (2 gms.)

followed four hours later by a similar dose. After this, two tablets (1 gm.) were given till fourteen to sixteen tablets (7-8 gms.) had been given. The subsequent dosage was varied with a view to noting the effects of various total dosages of the drug. Four cases received less than a total of eighteen tablets (9 gms.); sixteen cases were given eighteen to twenty-six tablets (9-13 gms.); eleven, twenty-seven to thirty tablets ( $13\frac{1}{2}$ -15 gms.); twenty-two cases thirty-one to thirty-six tablets ( $15\frac{1}{2}$ -18 gms.); eleven, thirty-seven to fifty tablets ( $18\frac{1}{2}$ -25 gms.); nineteen cases received over 25 gms.

In cases where oxygen was thought advisable in the early stages, it was given freely by means of a nasal catheter.

Sedatives were administered as the need for them arose. In some cases a local application, such as anti-phlogistine, was applied to the chest to relieve pain in the early days of the illness.

During the administration of the drug, sulphur-containing foods, such as eggs, were avoided, as were such aperients as magnesium sulphate.

Throughout the course of treatment watch was kept for the appearance of toxic symptoms and efforts

were made to overcome them as they appeared. A white blood count was made on all patients on the day of admission and in most at an interval of not more than three to four days and again towards the tenth day after admission.

Where complications arose, they were dealt with in the usual manner and in certain cases further doses of M. & B. 693 were administered.

Physical examination of the chest was carried out at frequent intervals throughout the course of the disease.



GROUP IV.

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within Hours	Tablets	1 day	3-5	later				
Walter S. G 9	55	3	R L L	101	24	12				-	Temp. tending up, Fall 10th day. Aspiration, Fluid	25	34
Mgt. McL. A 10	36	Type 4 3	R U L	28			15,800			Violent vomiting	Drug stopped. Temp. by lysis 9th	16	24
David M. G 2	44	Type 14 4	R L L	70	12	10	9,000		4,600		Temp. rose 1 day later, falling in 24 hrs. Rose later, 20 oz. fluid	?	22
James I. K 5	15	Type 19 1	L L L	18	8	8	7,800					10	14 Convals. <sup>t</sup>
Jennie E. K 10	38	Type 13 3	R L L	80			12,000	11,200		Vomiting Cyanosis	Temp. fell 8 day No response	Not up	14
Peter B. L 2	15	Type 4 2	R L L	46	18	12	30,000				Temp. rose after 24 hrs., falling in 48 hrs	14	17 Convals. <sup>t</sup>
James L. L 3	57	Type 5 2	R U L R M L	42	20	6	24,800					Not up	14
Mary S. B 13	21	Type 5 4	R L L	48	24	12	17,000	14,000				11	14
Thomas D. C 9	64	Type 9 1	R L L	16	18	10	13,400		10,400	Vomiting Stop M & B 693.	Urethral stricture, Haematuria, Cystoscopic examination revealed papilloma of bladder	24	61 Delay Resolution, X-ray.
Wesley J. C 5	14½	Type 16 3	R L L	30	24	10	13,000	6,600				18	26
Andrew L. D 2	15	Type 7 4	L L L	30		12	30,000	9,200		Vomiting 1st day M & B 693. continued			19

GROUP IV (contd.).

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	later				
Lawrence A. D 5	36	Type 9 1	R L L	34	24	20	19,800			Cyanosis	Some delay resol. Temp. tending up 11th day.		11 Convals. <sup>t</sup>
William B. D 8	28	Type 12 4	R M L	32	24	10	25,400		9,800			13	18
James Mc. K 1	19	Type 7 4	L L L	26	24	10	8,600					10	14
Alfred D. F 6	51	Type 4 1	L L L	26	24	8	17,000	7,000				21	26
Alex. <sup>r</sup> G. M 4	44	Type 5 3	L L L	22	14	10	15,800	11,000	6,200	Mild vomiting		18	26

TYPE I.

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	later				
Hugh D. K 2	52	2	R L L	50	72	14	16,800				Very toxic on admission	10	16 Convuls. <sup>t</sup>
William D. K 4	60	1	L L L	70	24	20	21,000					11	12
James N. L 1	30	2	R L L	42	24	22	21,400					10	12
Charles C. L 4	26	5	L L L	48	24	14	12,800					Not up	12, home to bed
Alex. M. D 3	31	2	L L L	33	36	22	24,000	25,000			Residual dullness on discharge	15	27
Catherine P. A 1	21	3	L L L	32	72	15	13,800					11	18
Annie O'D. E 9	19	3	R L L	32	24	16	19,600	16,000				19	39 No reason apparent



TYPE II.

Name & NO.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
Cissie McA. B 12	30	3	R L L	10	24	10	16,000			Vomiting	7 mths. pregnant.	10	13
John McB. A 9	22	3	R L L	36	24	24	16,200			-	-	-	16 Convals. <sup>t</sup>
Henry R. A 8	27	2	L L L	36	24	16				-	R L L Pneumonia developed 4 days later. No re-action M & B 693	42	47
Robert T. A 7	46	2	R U L L L L	28	24	16	24,000	-	14,000	-	Died cardiac failure after response M & B 693	-	Death
Angus McD. A 4	24	5	L U L	28	10	12	13,800			-		12	21
Frank D. F 2	18	4	R L L	32	12	12	15,000	5,400		-		16	19
Anthony G. E 12	37	2	R L L	34	24	12	8,000	6,000		-		18	24
Robert W. E 11	66	4	L L L	36	-	20	31,000		8,800		Delayed resolution	22	29 Convals. <sup>t</sup>
John D. E 8	16	3	L L L	36	36	20	13,800	7,000		-		12	16 Convals. <sup>t</sup>
Andrew H. E 6	13½	2	R U L	40	24	14	12,400	7,200		-		17	19
John T. D 9	28	3	R L L	30	24	14	8,800		6,700				14
Mrs Jeanie R. D 6	16	4	L L L	32	24	12	14,000		19,800	-		No	16



TYPE II (Contd.)

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
Bernard McK. D 4	15	1	R L L R U L R M L	32	24	16	20,000		20,000	Vomiting	Boils	18	38
Charles A. D 2	22	2	L L L	22 +40	12	10	24,600	10,400		Vomiting Stop drug	Temp. rose 6th day for 24 hrs. Given 40 more M & B 693 Tablets.	12	13
James B. C 4	23	2	R L L	30	32	14	19,600	8,600		Vomiting, M & B continued		18	25
Jessie R. C 7	54	2	R L L	36	24	12	18,600		11,200	Cyanosis	Atelectasis Rt. U. L. Old standing?	22	34
George R. C 8	51	6	L L L	20	24	10	17,000		8,800	Cyanosis Nausea	-	22	30
David B. C 11	62	4	R L L	23	24	14	11,000		7,200	Vomiting Stop M & B 693	I.V. saline Very ill on admission	16	26
Thomas G. H 15	60	3	R M L R L L	68	24	10	11,500		12,000	-	Delayed resolution	13	22 Convals. <sup>t</sup>
Thomas A. H 12	15	3	R L L	30	24	12	10,000		10,800	-	-	12	25
Charles S. H 10	24	3	L L L	72	24	16	14,000	14,000		-	Fluid Rt. base Empyema	Surgeon	
John G. G 6	40	3	L U L	62	24	10	9,600	9,000		-	-	10	15
Alex. B. B 19	29	5	R L L	31	12	14	20,400		13,400		Empyema after interval		20
John P. B 16	22	2	L L L	28	24	16	27,000			-		17	20
Joshua L. B 14	43	4	R L L	12	Marked general bronchitis: toxic.							Death	

TYPE II (Contd.)

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
Charles H. K 11	16	2	L L L	63	12	8	17,500			-	-	11	14 Convals. <sup>t</sup>
Thomas G. K 9	38	2	L L L	46	24	18	15,200		11,000	-	-	15	23
Samuel B. K 8	63	4	L L L	58	Temp. never high		9,500	11,200	9,100		Retention urine, Toxic old man		Death
Arthur H. K 7	22	2	R U L	80	24	18	6,200	21,800	17,600	-	Temp. rose after 24 hrs., fell 5 days after admis- sion	Not up	14 Convals. <sup>t</sup>
William McT. K 6	46	3	R L L	56	24	10	11,000		11,200	-	-	Not up	9 Convaless. <sup>t</sup>
George G. K 3	51	1	R L L	60	24	14	17,600			-	Very ill on admission	13	16
Mary B. M 1	13	4	R U L	10	24	10	10,000	12,400	9,800	-	Undernourished	23	34
Jessie B. M 2	17	5	L L L	35	13	8	14,600		9,600	-	-	16	18 Convals. <sup>t</sup>

TYPE III.

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
George McL. A 2	67	4	R U L	30	12	8	14,000	16,000		-	Delirious after fall of temp.	7	20
Charles G. A 3	56	4	R L L	42	24	14				-	Temp. rose 24 hrs. later, continued 14 days despite M & B 693.	37	45
James D. A 6	62	3	R U L	36	48	28	11,600					13	21
John M. G 3	63	6	L L L	49	24	20	9,600	9,000					26
Jean D. C 12	40	5	Both bases	22	24	10	11,000		6,200			15	19
Leonard R. H 14	48	4	R U L R L L	54	24	16	12,200		8,500			13	15
Alex. McK. G 8	60	2	R L L	76	24	20	21,000		8,400			15	21



STREPTOCOCCAL.

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
James C. H 16	26	4	R M L	20	12	8	7,800		5,200	-	-	13	20
Charles R. C 3	52	1	R L L	31	Temp. never rose beyond normal		18,000		9,800	Nausea Cyanosis	(Carcinoma Penis)	16	17 Convals. <sup>t</sup>
Thady McN. F 1	19	3	L L L	44	24	14	12,000	8,200		-	-	13	17 Convals. <sup>t</sup>
Jeanette McD. E 5	30	2	R L L	32	36	20	13,000		8,000	-	-	19	26
Mrs Jane S. E 10	26	1	R L L	52	Temp. did not fall till 6 days after & then tended to evening rise		40,000		12,000	Cyanosis	Delayed resolution		13 Convales. <sup>t</sup>



MIXED INFECTIONS.

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
Catherine T. D 7	18	Type I & 16 3	L L L	42		42	28,100		9,600	-	-	18	24
Joseph L. E 14	17½	18 & I 2	L L L	30	24	10	11,000		5,000	-	-	?	17
James F. B 15	17	I & 6 2	L L L	60	48	26	12,400	16,400		-	-	14	20
Arthur R. B 18	44	1,6,20, 22. 1	R L L	84	48	30	7,200		7,600	Cyanosis	Temp. rose 6th day, M & B 693 given for further 2 days, fall.		14

NOT TYPED.

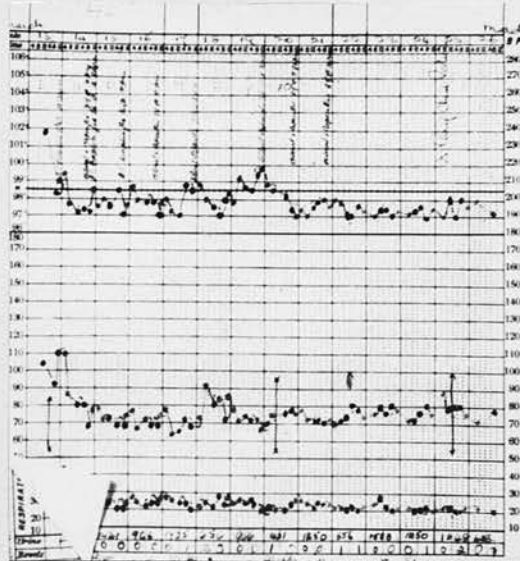
Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
Robert W. G 1	18	4	L L L	36	24	10	12,000			-	-	?	10 days
Robert B. G 7	43	2	R L L	65		22					Axillary adenitis probable cause of rise in temp. Further 41 tablets M & B 693	28	34
Thomas McH. B 17	14	4	R L L	13	24	13	18,000		9,100			16	26
Magnus R. H 13	19	4	R M L R L L	39	24	10	10,000		6,300			15	24
John McR. H 11	15	3	R M L R L L	78	12	12	20,200	19,400				11	21
Joseph P. C 6	61	2	R L L	24	24	12	15,800	16,600			Died from cancer pharynx with liver secondaries	Responded to M & B 693. N.B. No organisms found.	
Mrs Ellen W. D 10	56	1	R L L	32	36	22	14,000					15	19
James G. E 4	21	2	R L L	26	24	10	8,400	8,000				10	13
Andrew G. E 7	46	2	L L L	32	24	18	7,500	23,600	11,200		Temp. rose 3 days later - no response M & B 693. Fell 5 days later.	18	26
Robert B. E 13	12	3	L L L	32	24	16	17,000		7,200	Vomiting		?	14
May L. A 11	66	3	L L L	28		10	14,000			-		16	21



51a.

NOT TYPED (Contd.).

Name & No.	Age	Day of Illness	Site	Total M & B	Temp. fell after M & B		White Blood Count			Toxic Symptoms	Complications	Up	Duration Stay
					within hours	Tablets	1 day	3-5	Later				
Lindsay R. M 3	81	1	L L L	19	9	8	7,400	9,600			Myocardial de- generation and coronary infarct "Old Age"	7	38
Robert D. A 5	35	2	R L L	30	72	24	14,200					13	24



Name: Walter S.

Case Letter: G 9.

Age: 55 years.

Sex: Male.

Admitted 13.3.39.

Day of Illness: Third.

History: Patient has had a cold for past week. On morning of 11.3.39 had severe pain in right side of chest.

Examination of Chest: Diminished expansion of right side. Dullness of right lower lobe, with coarse friction. Breath sounds inaudible.

Sputum: Type 8 Pneumococcus.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.8° F.	97.2	97.6
Pulse	104 p. min.	80	72
Respiration	42 " "	20	24
Blood pressure	84/54		



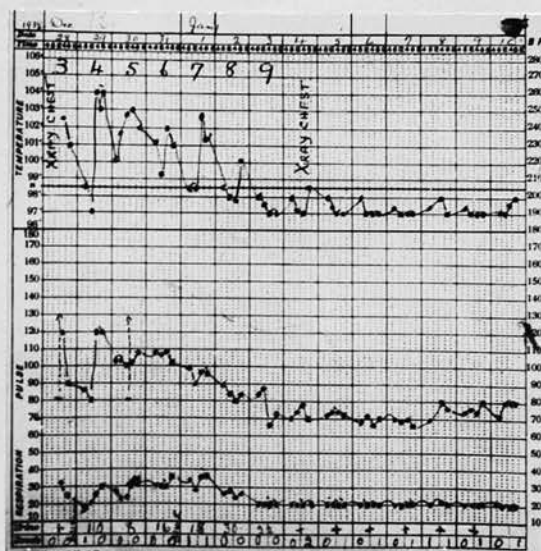
White Blood Count: On admission, 11,000 per c.cm.  
20.3.39, 14,400 per c.cm.

X-ray: Pneumonic consolidation of right base.  
25.3.39: Fluid at right base.

M. & B. 693: Total dosage - 101 tablets - 50.5 gms.  
Fall in temperature after 12 tablets.

Complications: Temperature had a tendency to remain  
above normal for ten days. Fluid was found  
to be present at right base, and this was  
removed. Patient made an uninterrupted  
recovery. Fluid sterile.

Discharge 16.4.39, after 34 days in hospital.  
Up on 25th day.



Name: Margaret McL.      Case Letter: A 10.

Age: 36 years.      Sex: Female.

Admitted 28.12.38.      Day of Illness: Third.

History: Two days before admission felt out of sorts and in the evening had a rigor followed by profuse sweating. A few hours later had a pain in the right side of her chest and a frequent painful cough.

Examination of Chest: Increased vocal fremitus in the right upper lobe. Diminished bronchial breathing and a few crepitations. Increased vocal resonance.

Sputum: Type IV.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.4°F.	104	103
Pulse	120 per min.	120	102
Respiration	32 " "	26	30
Blood pressure	130/80		

White Blood Count: On admission, 15,800, per c.cm.

X-ray: Patch of consolidation in upper part of right lung.

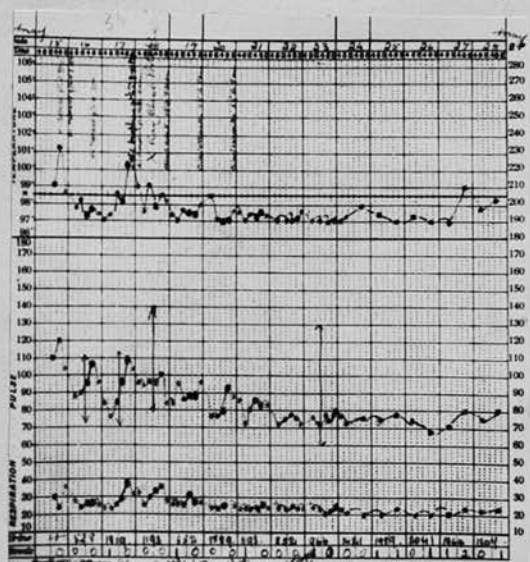
4.1.39: Confirmed pneumonia.

M. & B. 693: Total dosage - 28 tablets - 14 grms.  
Temperature fell by lysis on the 9th day of illness.

Toxic Symptoms: Violent sickness after the second day, drug discontinued.

Discharged 21.1.39, having been out of bed from 16th day.

Duration of stay in hospital - 24 days.



Name: Daniel M.

Case Letter: G 2.

Age: 44 years.

Sex: Male.

Admitted 15.5.39.

Day of illness: 4th.

History: Well till seven days ago when he felt sick and dizzy. Woke next morning feeling sore all over and had a shivering fit. Three days ago developed pain in chest.

Examination of Chest: Impaired percussion of right lower lobe. Breath sounds faint. Increased vocal resonance, and friction rales.

Sputum: Type 14.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	97.2	98.2
Pulse	110 p. min.	96	96
Respiration	30 p. min.	26	30
Blood Pressure	110/72		



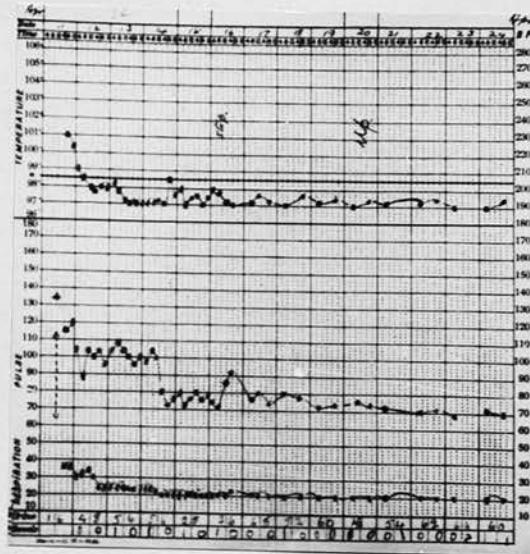
White Blood Count: On admission, 9,000 per c.cm.  
31.5.39, 4,600 per c.cm.

X-ray: 18.5.39 - Consolidation and some fluid at  
right base.  
30.5.39 - Unresolved pneumonia; fluid present.

M. & B. 693: Total dosage - 70 tablets - 35 grms.  
Temperature fell after 10 tablets, but varied  
for two days after.

Complications: The temperature rose on 29.5.39; the  
chest was explored, with the removal of 20 ozs.  
fluid, containing B. Proteus.

Discharge on 6.6.39, after 22 days in hospital.



Name: James I.

Case Letter: K 5.

Age: 15 years.

Sex: Male.

Admitted 11.4.39.

Day of illness: 1st.

History: On day of admission complained of pain in left side, while at work.

Examination of Chest: Restricted movement and dullness at left base. Bronchial breathing with fine crepitations, with friction above this.

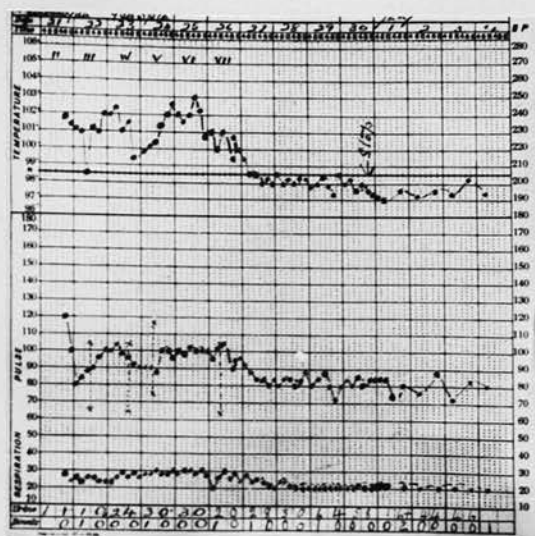
Sputum: Type 19.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	98	97
Pulse	116 p. min.	104	96
Respiration	36 p. min.	24	24
Blood Pressure	112/64		

White Blood Count: On admission, 7,800 per c.cm.

M. & B. 693: Total dosage - 18 tablets - 9 grms.  
Fall in temperature after 8 tablets, i.e. 8  
hours after admission.

Discharge 25.4.39 to Convalescent Home after 14 days  
in hospital. Up on 10th day.



Name: Mrs Jenny E.      Case Letter: K 10.

Age: 38 years.      Sex: Female.

Admitted 21.6.39.      Day of illness: 3rd.

History: On 19.6.39 patient had a shivering fit and pain in the back. The pain spread to the abdomen and she was sent to Hospital as a surgical emergency.

Examination of Chest: Limitation of movement on right side. Dullness of middle right lobe with bronchial breath sounds.

Sputum: Type 13.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.8°F	101	99.4
Pulse	120 p. min.	96	92
Respiration	28 p. min.	24	28
Blood Pressure	104/64		



White Blood Count: On admission, 12,000 per c.cm.  
26.6.39, 11,200 per c.cm.

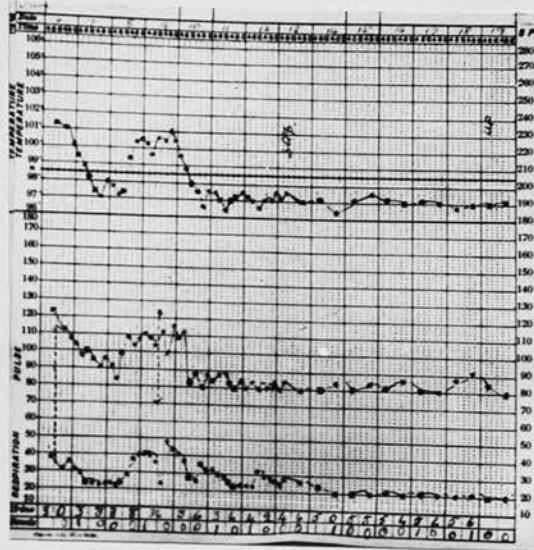
X-ray: Inflammatory process of right lower lobe in  
upper part.

M. & B. 693: Total dosage - 80 tablets - 40 grms.  
Fall in temperature on 8th day.

Toxic Symptoms: Vomiting, slight cyanosis.

Duration of stay in Hospital - 14 days.

Discharged 4.7.39: not up.



Name: Peter B. Case Letter: L 2.

Age: 15 years. Sex: Male.

Admitted 6.6.39. Day of illness: 2nd.

History: On morning before admission was suddenly sick; this was followed in the evening by a pain in the right side on coughing; blood-stained sputum.

Examination of Chest: Diminished expansion and dullness at right base. Bronchial breathing with crepitations. Vocal resonance increased.

Sputum: Type 4 (Group IV).

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.4°F	98.2	97.4
Pulse	122 p. min.	100	100
Respiration	38 p. min.	30	34
Blood pressure	112/64		

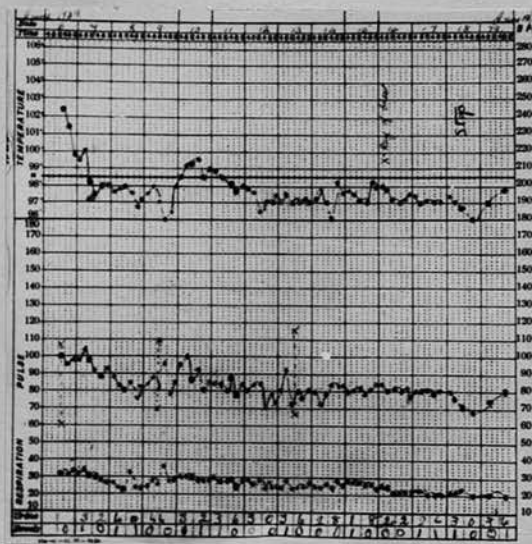
White Blood Count: On admission, 30,000 per c.cm.

M. & B. 693: Total dosage - 46 tablets - 23 grms.  
Fall in temperature after 12 tablets,  
i.e. 18 hours.

Complications: Temperature rose again 24 hours later  
and fell in 48 hours.

Discharged on 23.6.39 to Convalescent House, after 17  
days in hospital.

Up on 14th day.



Name: James L.      Case Letter: L 3.

Age: 57 years.      Sex: Male.

Admitted 6.6.39.      Day of illness: 2nd.

History: Two days before admission had headaches and general malaise. On day before admission pain in right side of chest: sputum blood-tinged.

Examination of Chest: Barrel-shaped; impaired movement, right side of chest; harsh vesicular breathing in upper part of right lung with fine crepitations; increased vocal resonance in this area.

Sputum: Type 5.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.4°F.	97.4	97.6
Pulse	100 p. min.	92	84
Respiration	32 p. min.	30	32
Blood Pressure	106/60		

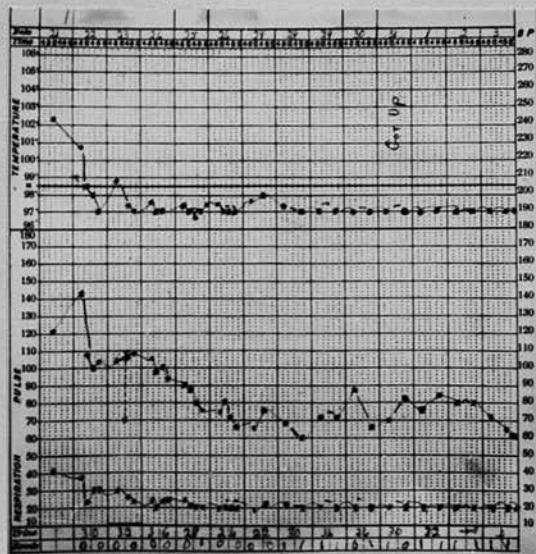


White Blood Count: On admission, 24,800 per c.cm.

X-ray: Partial consolidation of upper  $\frac{2}{3}$  of right lung field.

M. & B. 693: Total dosage - 42 tablets - 21 grms.  
Fall in temperature after 6 tablets, i.e.  
within 20 hours.

Discharged 20.6.30 to Convalescent Home after 14 days  
in hospital.



Name: Mary S.      Case Letter: B 13.

Age: 21 years.      Sex: Female.

Admitted 21.12.38.      Day of illness: 4th.

History: Three days ago felt shivery and this was followed by a sharp pain in the right side of the chest, and a frequent, painful cough.

Examination of Chest: Dullness at right base with diminished bronchial breathing and occasional crepitations.

Sputum: Type 5.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.4°F.	98.5	98.2
Pulse	120 p. min.	108	104
Respiration	40 p. min.	24	28
Blood Pressure	110/70		

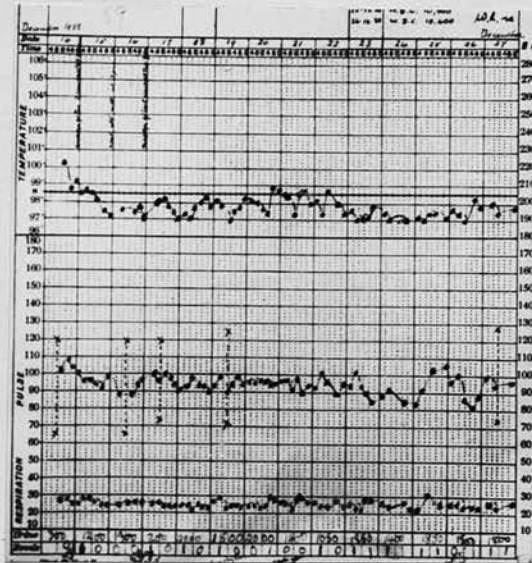
67.

White Blood Count: On admission, 17,000 per c.cm.  
24.12.38, 14,000 per c.cm.

M. & B. 693: Total dosage - 48 tablets - 24 grms.  
Fall in temperature after 12 tablets, i.e.  
within 24 hours.

Discharged 4.1.39 after 14 days in hospital.

Up on 11th day.



Name: Thomas D.      Case Letter: C 9.

Age: 64 years.      Sex: Male.

Admitted 14.12.38.      Day of illness: 1st.

History: Generalised aches and pains for three days, followed by right sided chest pain and cough shortly before admission.

Examination of Chest: Impaired movement and dull percussion note at right base, with bronchial breathing.

Sputum: Type 9.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.2°F.	98.2	97.4
Pulse	100 p. min.	94	88
Respiration	28 p. min.	26	26
Blood Pressure	120/66		



White Blood Count: On admission, 13,400 per c.cm.  
17.12.38, 14,000 " "  
26.12.38, 10,400 " "

X-ray: Pneumonia of right lower lobe.  
28.1.39: Delayed resolution of an inflammatory process.

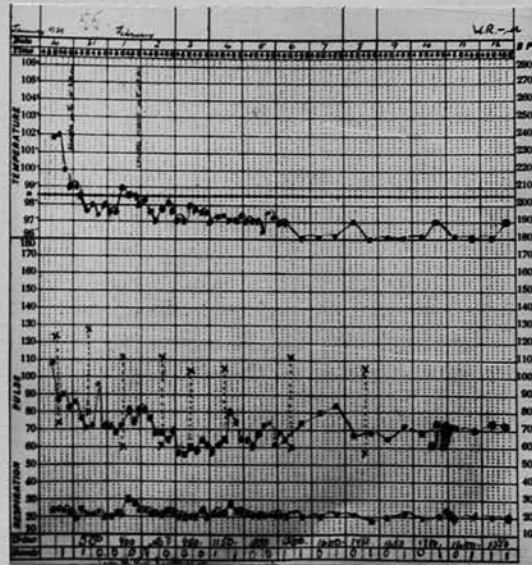
M. & B. 693: Total dosage - 16 tablets - 8 grms.  
Fall in temperature after 10 tablets.

Toxic symptoms: Vomiting. Treatment stopped.

Complications: Urethral stricture and papilloma of bladder revealed by cystoscopic examination.

Discharged 17.2.39 after 61 days in hospital.

Up on 24th day.



Name: Wesley J.      Case Letter: C 5.

Age: 14½ years.      Sex: Male.

Admitted 30.1.39.      Day of illness: 3rd.

History: Two days ago developed pain across front of chest, made worse on coughing, and cough produced a green frothy sputum.

Examination of Chest: Impaired expansion and percussion note at right base, with faint breath sounds and fine crepitations.

Sputum: Type 16.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	97.6	99
Pulse	110 p. min.	70	72
Respiration	24 p. min.	22	22
Blood pressure	122/72		

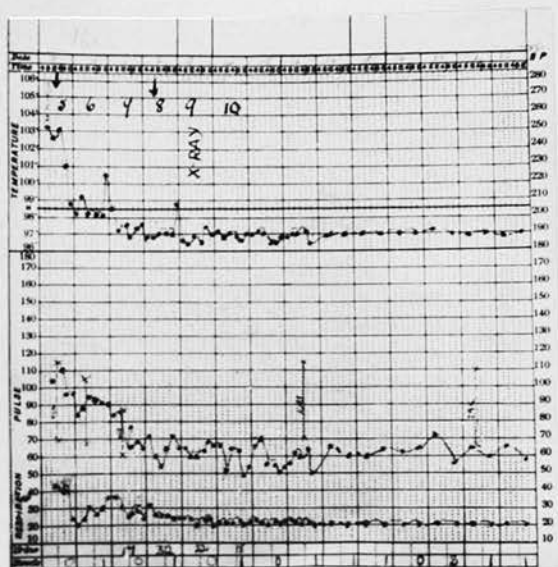
71.

White Blood Count: On admission, 13,000 per c.cm.  
1.2.39, 7,200 " "  
4.2.39, 6,600 " "

M. & B. 693: Total dosage - 30 tablets - 15 grms.  
Fall in temperature after 10 tablets, i.e.  
within 20 hours.

Discharged on 25.2.39, after 26 days in hospital.

Up on 18th day.



Name: Andrew L.      Case Letter: D 2.

Age: 15 years.      Sex: Male.

Admitted 9.3.39.      Day of illness: 4th.

History: Three days previous to admission, complained of sharp stabbing pain in left side of chest, accompanied by a short painful cough.

Examination of Chest: Stony dullness at left base; loud tubular breathing; vocal resonance markedly increased.

Sputum: Type 7.

	On Admission	Treatment with M & B 693	
		After 24 hours.	After 48 hrs.
Temperature	103.2°F.	99.2	97.2
Pulse	110 p. min.	88	86
Respiration	42 p. min.	24	30
Blood Pressure	114/70		



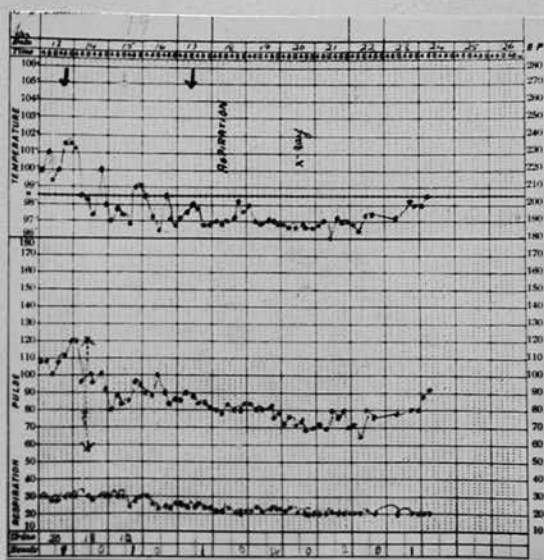
White Blood Count: On admission, 30,000 per c.cm.  
14.3.39, 9,200. " "

X-ray: 13.3.39 - Inflammatory process of left base,  
unresolved.

M. & B. 693: Total dosage - 30 tablets - 15 grms.  
Fall in temperature after 12 tablets.

Toxic Symptoms: Vomiting on first day of administration.

Discharged 28.3.39 after 19 days in hospital.



Name: Lawrence A.      Case Letter: D 5.

Age: 36 years.      Sex: Male.

Admitted 13.1.39.      Day of illness: 1st.

History: Several previous attacks of pneumonia;  
had a cold for fourteen days; two days  
before admission, fractured 11th rib;  
on day of admission, severe chest pain.

Examination of Chest: Dullness both bases; breath  
sounds faint; fine crepitations both  
bases.

Sputum: Type 9.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100°F.	99.6	97
Pulse	110 p. min.	96	80
Respiration	30 p. min.	30	30
Blood Pressure	120/60		

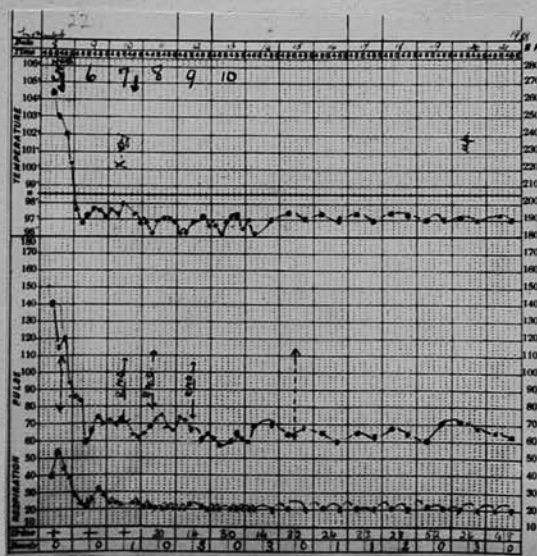
White Blood Count: On admission, 19,800 per c.cm.

X-ray: Consolidation of right lower lobe.  
30.1.39: Lung field clear; right costo-phrenic angle obscured.

M. & B. 693: Total dosage - 34 tablets - 17 grms.  
Fall in temperature after 20 tablets, i.e.  
24 hours after admission.

Toxic symptoms: Cyanosis.

Discharged 24.1.39 to Convalescent Home after 11 days  
in hospital.



Name: William B.      Case Letter: D 8.

Age: 29 years.      Sex: Male.

Admitted 8.11.38.      Day of illness: 4th.

History: Patient well till four days before admission, when he had a shivering fit. Next day he complained of pain in the middle of the back, aggravated by coughing and breathing.

Examination of Chest: Dullness in right axilla with bronchial breath sounds.

Sputum: Type 12.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	104.4°F.	97.2	98
Pulse	140 p. min.	60	74
Respiration	40 p. min.	22	22
Blood Pressure	110/80		



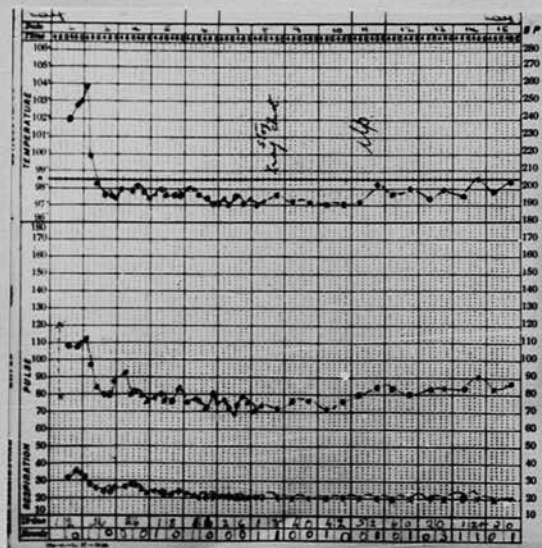
White Blood Count: On admission, 25,400 per c.cm.  
25.11.39, 9,800 " "

X-ray: Consolidation of right middle lobe.  
25.11.38 - clear.

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 10 tablets, i.e.  
within 24 hours.

Discharged on 25.11.39 after 18 days in hospital.

Up on 13th day.



Name: James McC.

Case Letter: K 1.

Age: 19 years.

Sex: Male.

Admitted 2.5.39.

Day of illness: 4th.

History: Pain in left side of chest since 29.4.39.

Examination of Chest: Diminished movement of left side; dullness and bronchial breathing, with fine crepitations.

Sputum: Type 7.

	On Admission	Treatment with M & B 693.	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	97.6	98.2
Pulse	110 p. min.	80	82
Respiration	32 p. min.	22	27
Blood Pressure	120/78		

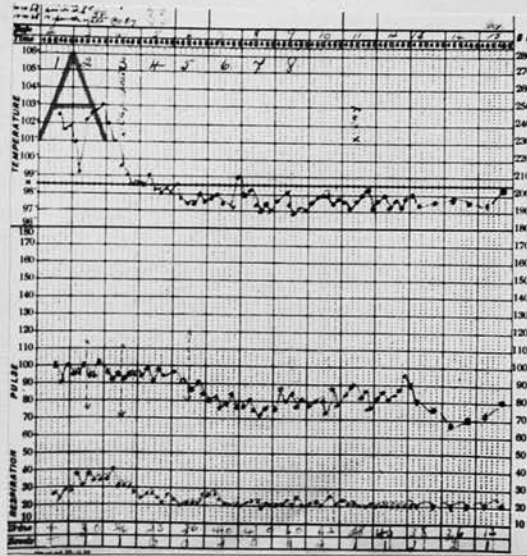
White Blood Count: On admission 8,600 per c.cm.

X-ray: 8.5.39 - Chest negative.

M. & B. 693: Total dosage - 26 tablets - 13 grms.  
Fall in temperature after 10 tablets i.e.  
within 24 hours.

Discharged 15.5.39 after 14 days in hospital.

Up ten days after admission.



Name: Alfred D.

Case Letter: F 6.

Age: 51 years.

Sex: Male.

Admitted 2.10.38.

Day of illness: 1st.

History: Wakened early on morning of admission with severe pain in the left side of chest, followed shortly by a slight cough, bringing up blood-tinged, frothy sputum.

Examination of Chest: Restricted movement, with impaired percussion note at left base; also bronchial breathing with a few fine crepitations.

Sputum: Type 4.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.5°F.	102.6	99
Pulse	100 p. min.	94	94
Respiration	26 p. min.	38	30
Blood Pressure	104/76		



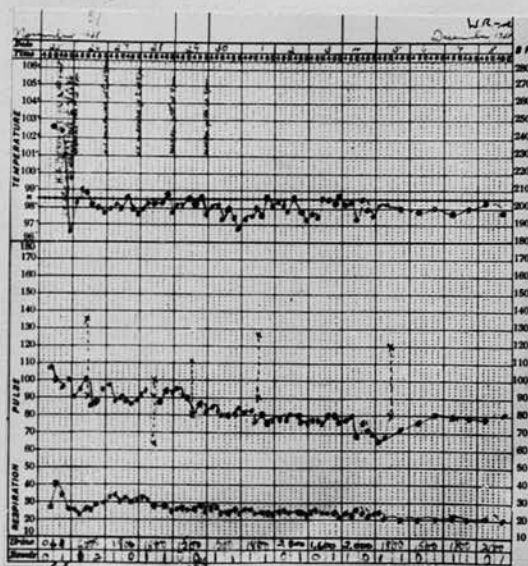
White Blood Count: On admission, 17,000 per c.cm.  
6.10.38, 7,000 " "

X-ray: Consolidation of lower half of left lung field.  
11.10.38: Inflammatory process fast resolving.

M. & B. 693: Total dosage - 26 tablets - 13 grms.  
Fall in temperature after 8 tablets, i.e.  
after 24 hours' administration, though treatment not started till 3.10.38.

Discharged 28.10.38 after 26 days in hospital.

Up on 21st day.



Name: Alexander G.      Case Letter: M 4.

Age: 44 years.      Sex: Male.

Admitted 25.11.38.      Day of illness: 3rd.

History: Three days before admission developed pain in the epigastrium; next morning had left-sided pain and cough, followed by constant severe headache.

Examination of Chest: Dullness on left side of chest with bronchial breathing; vocal fremitus and vocal resonance increased.

Sputum: Type 5.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.6°F.	98.8	98
Pulse	108 p. min.	100	90
Respiration	40 p. min.	26	30
Blood Pressure	134/90		

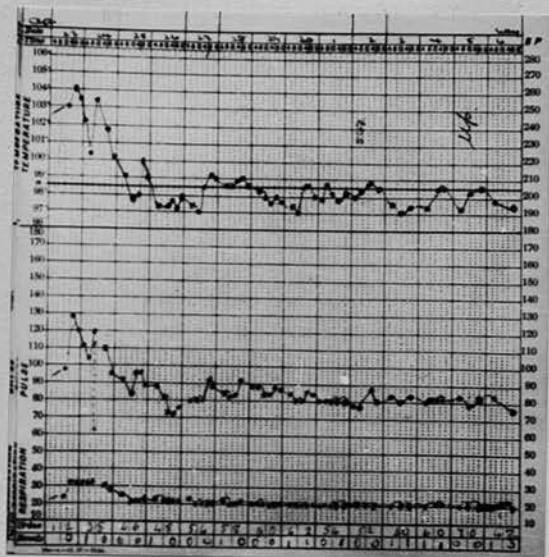
White Blood Count: On admission - 15,800 per c.cm.  
29.11.38 - 11,000 " "  
2.12.38 - 6,200 " "

M. & B. 693: Total dosage - 22 tablets - 11 grms.  
Fall in temperature after 10 tablets.

Toxic Symptoms: Mild vomiting.

Discharged 21.12.38 after 26 days in hospital.

Up on 18th day.



Name: Hugh D. Case Letter: K 2.

Age: 52 years. Sex: Male.

Admitted 23.4.39. Day of illness: 2nd.

History: On 22.4.39 patient developed a pain in the small of the back, with a cough which aggravated the pain, and also produced a rusty sputum.

Examination of Chest: Restricted movement of right base; dullness of right lower lobe, with distant bronchial breathing.

Sputum: Type I.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103°F.	99	97.4
Pulse	98 per min.	92	88
Respiration	24 p. min.	25	22
Blood Pressure	112/62		



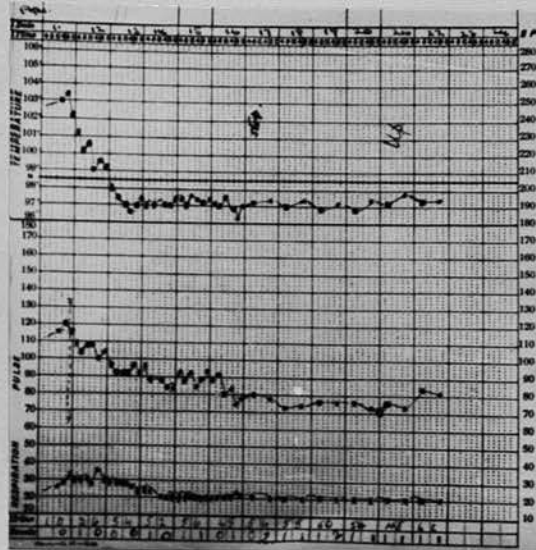
White Blood Count: On admission, 16,800.

X-ray: 3.5.39 - Old standing pleural thickening.

M. & B. 693: Total dosage - 50 tablets - 25 grms.  
Fall in temperature after 14 tablets.

Discharged 9.5.39 to Convalescent Home after 16 days  
in hospital.

Up on 10th day.



Name: William D.      Case Letter: K 4.

Age: 60.      Sex: Male.

Admitted 11.4.39.      Day of illness: 1st.

History: On evening before admission, shivering and vomiting; in the early hours of this morning pain in the upper half of left chest, with cough.

Examination of Chest: Limitation of movement at left base, with impaired percussion. Friction heard at this area and harsh vesicular breathing.

Sputum: Type I.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103°F.	99	96.6
Pulse	116 p. min.	108	92
Respiration	26 p. min.	28	28
Blood Pressure	132/64		

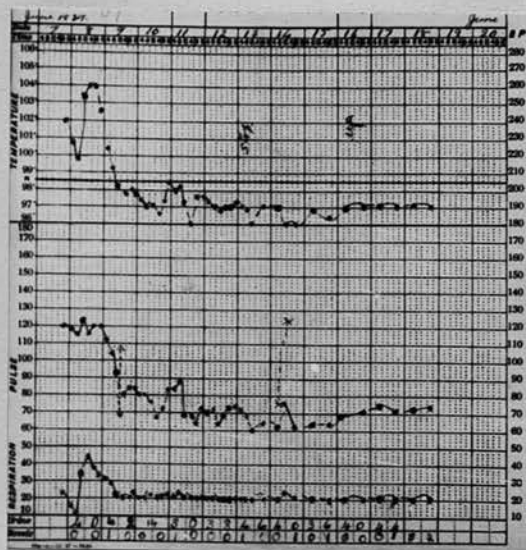
White Blood Count: On admission, 21,000 per c.cm.

X-ray: 13.4.39 - Consolidation below left hilum.

M. & B. 693: Total dosage - 70 tablets - 35 grms.  
Fall in temperature after 20 tablets, i.e.  
within 24 hours.

Discharged 22.4.39 to Convalescent Home after 12 days  
in hospital.

Up on 11th day.



Name: James N.

Case Letter: L 1.

Age: 30 years.

Sex: Male.

Admitted 7.6.39.

Day of illness: 2nd.

History: Cough for two days before admission, with headache and general malaise.

Examination of Chest: Pleural rub over right lung anteriorly and inferiorly.

Sputum: Type I.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	102.6	98
Pulse	120 p. min.	120	84
Respiration	22 p. min.	36	20
Blood Pressure	110/70		

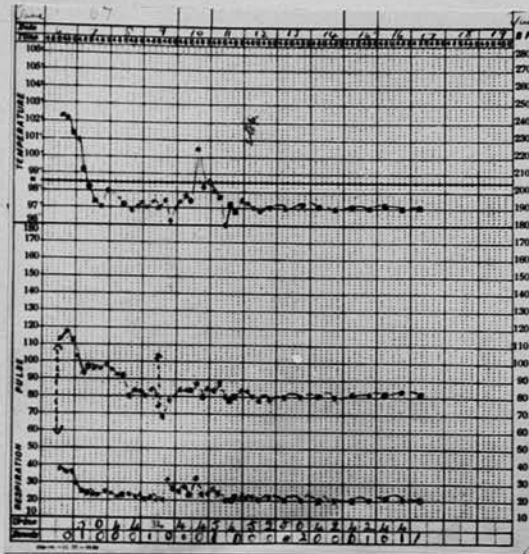


White Blood Count: On admission, 21,400 per c.cm.

M. & B. 693: Total dosage, 42 tablets - 21 grms.  
Fall in temperature after 22 tablets i.e.  
24 hours after admission.

Discharged 28.6.39, after 12 days in hospital.

Up on 10th day.



Name: Charles C.      Case Letter: L 4.

Age: 26 years.      Sex: Male.

Admitted 6.6.39.      Day of illness: 5th.

History: On 2.6.39 had severe pain in left side of chest, with giddiness and sweating. On day before admission had a cough and blood-stained sputum.

Examination of Chest: Diminished movement and dullness over left base; bronchial breathing with crepitations.

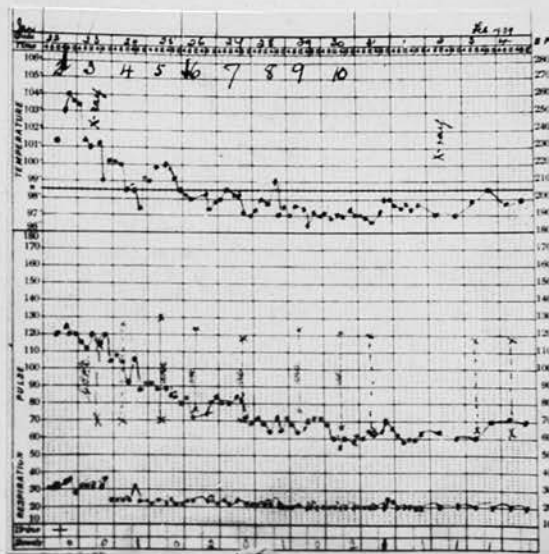
Sputum: Type I.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.3°F.	97.4	96.8
Pulse	112 p. min.	96	80
Respiration	38 p. min.	24	22
Blood Pressure	110/60		

White Blood Count: On admission, 12,800 per c.cm.

M. & B. 693: Total dosage - 48 tablets - 24 grms.  
Fall in temperature after 14 tablets.

Discharged 17.6.39, after 12 days in hospital.



Name: Alexander M.      Case Letter: D 3.

Age: 31 years.      Sex: Male.

Admitted 22.1.39.      Day of illness: 2nd.

History: Patient has had a cold for seven days.  
Yesterday he had several shivering fits  
and late last night he took a severe  
pain in the left side of his chest.

Examination of Chest: Dullness of left lower lobe;  
increased vocal fremitus and vocal  
resonance; diminished breath sounds.

Sputum: Type I.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.2°F.	99	97.4
Pulse	120 p. min.	120	88
Respiration	32 p. min.	36	24
Blood Pressure	112/70		



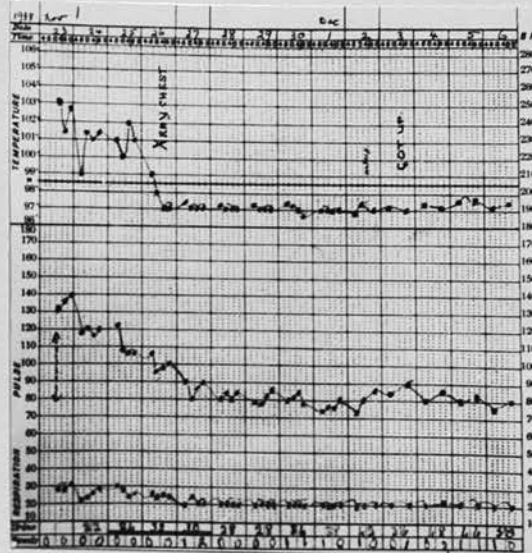
White Blood Count: On admission, 24,000 per c.cm.  
23.1.39, 35,000 " "

X-ray: 23.1.39 - Left lower lobe consolidation.  
2.2.39 - Consolidation outwards and down to  
left hilum.  
6.3.39 - Clear.

M. & B. 693: Total dosage - 33 tablets - 16.5 grms.  
Fall in temperature after 22 tablets, i.e.  
36 hours.

Discharged 18.2.39 after 27 days in hospital.

Up on 15th day.



Name: Catherine P.      Case Letter: A 1.

Age: 21 years.      Sex: Female.

Admitted 23.11.38.      Day of illness: 3rd.

History: Two days before admission felt out of sorts and shivery. This was followed in a few hours by a sharp pain in the left side of the chest.

Examination of Chest. Dullness at left base with bronchial breath sounds; increased vocal fremitus and resonance.

Sputum: Type I Pneumococcus.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103°F.	101	102
Pulse	130 p. min.	116	106
Respiration	30 p. min.	26	26
Blood Pressure	108/80		

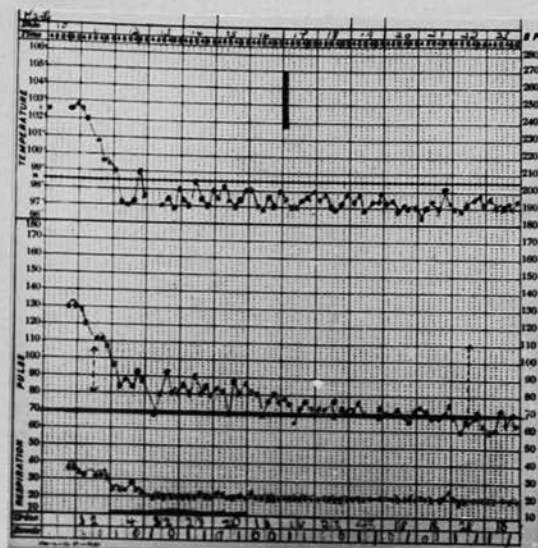
White Blood Count: On admission, 13,800 per c.cm.

K-ray: Consolidation of left lower lobe.

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 15 tablets, i.e.  
after 3 days - tablets being given only one  
4-hourly.

Discharged 10.12.38, after 18 days in hospital.

Up on 11th day.



Name: Annie O'D.

Case Letter: E 9.

Age: 19 years.

Sex: Female.

Admitted 10.3.39.

Day of illness: 3rd.

History: Two days prior to admission patient felt shivery and developed pain in right side of chest.

Examination of Chest: Dullness over right lower lobe; high pitched bronchial breathing in lower part of right lobe.

Sputum: Type I.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.8°F.	99.6	99
Pulse	130 p. min.	112	92
Respiration	38 p. min.	32	24
Blood Pressure	108/80		



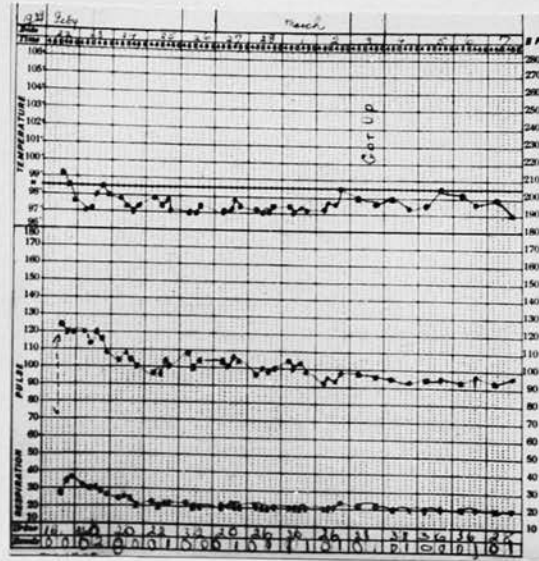
White Blood Count: On admission, 19,600 per c.cm.  
14.3.39, 16,000 " "

X-ray: 5.4.39 - Clear.

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 16 tablets, i.e.  
24 hours later.

Discharged on 7.4.39, after 39 days in hospital.

Up on 19th day.



Name: Mrs Cissie McA.      Case Letter: B 12.

Age: 30 years.      Sex: Female.

Admitted 22.2.39.      Day of illness: 3rd.

History: Two days before admission felt out of sorts and was troubled by a sharp pain in the right side of the chest. The following day the pain was much worse and aggravated by coughing and breathing; also had a sticky blood-stained sputum.

Examination of Chest: Dullness on right side of chest with bronchial breathing; vocal fremitus and vocal resonance increased.

Sputum: Type II Pneumococcus.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	99.4°F.	98	97
Pulse	126 p. min.	120	104
Respiration	34 p. min.	30	25
Blood Pressure	118/72		

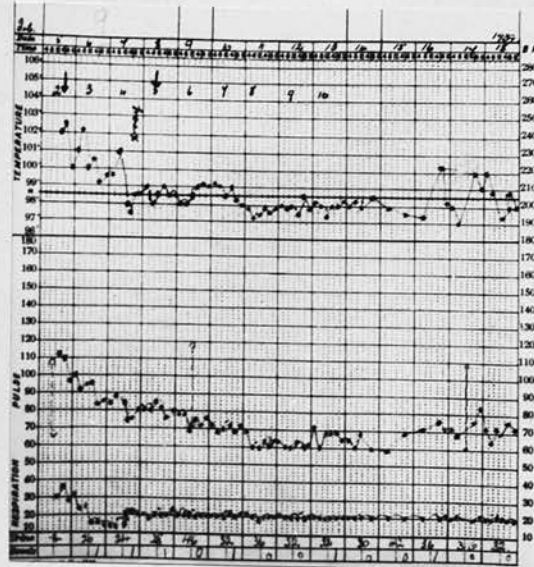
White Blood Count: On admission, 16,000 per c.cm.

M. & B. 693: Total dosage - 10 tablets - 5 grms.  
Fall in temperature after 10 tablets, i.e.  
24 hours.

Complication: Seven months pregnant, but the foetus  
had good heart beats throughout.

Discharged 7.3.39 after 13 days in hospital.

Up on 10th day.



Name: John McB.

Case Letter: A 9.

Age: 22 years.

Sex: Male.

Admitted 5.2.39.

Day of illness: 3rd.

History: Two days before admission felt out of sorts and shivery. This was followed at night by a sharp pain in the right side of the chest, later associated with a dry, painful cough.

Examination of Chest: Dullness on percussion and bronchial breathing at right base. Vocal resonance increased.

Sputum: Type II Pneumococcus.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	100.6	97.4
Pulse	112 p. min.	96	74
Respiration	30 p. min.	16	20
Blood Pressure	108/64		

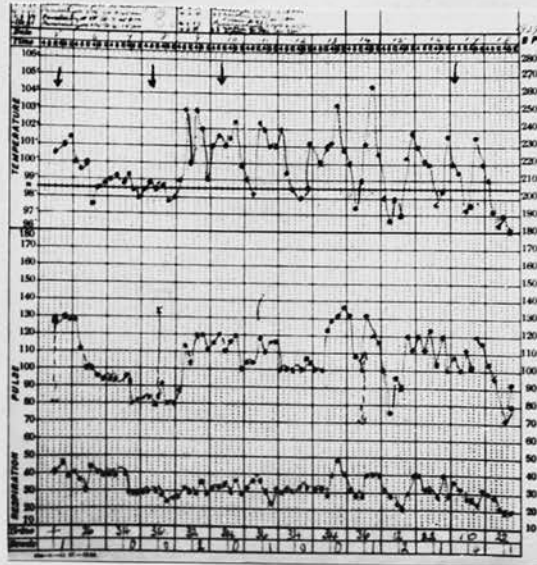


White Blood Count: On admission, 16,200 per c.cm.

X-ray: Pneumonic consolidation of right lower lobe.

M. & B. 693: Total dosage - 36 tablets - 18 grms.  
Fall in temperature after 24 tablets, i.e. in  
36 hours.

Discharged 21.2.39 to Convalescent Home after 16 days  
in hospital.



Name: Henry R.

Case Letter: A 8.

Age: 27 years.

Sex: Male.

Admitted 5.2.39.

Day of illness: 3rd.

History: Two days before admission, contracted a severe attack of "influenza", with cough and pain in the chest.

Examination of Chest: Impaired movement with dullness on percussion of left base. Vocal fremitus and vocal resonance increased; bronchial breathing.

Sputum: Type II.

	On Admission	Treatment with M & B 693.	
		After 24 hrs.	After 48 hrs.
Temperature	100.6°F.	100	98.8
Pulse	130 p. min.	100	96
Respiration	42 p. min.	30	40
Blood Pressure	110/70		

White Blood Count: On admission, 24,000 per c.cm.  
                                     8.2.39, 20,000   "   "  
                                     11.2.39, 26,000   "   "

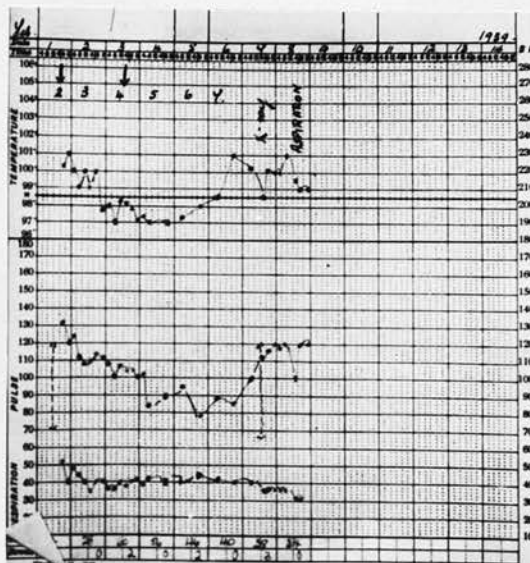
X-ray: Consolidation of left base.

M. & B. 693: Total dosage - 36 tablets - 18 grms.  
                                     Fall in temperature after 16 tablets, i.e.  
                                     within 24 hours.

Complication: Four days after temperature had fallen, it rose to 103°F. and it was found that the pneumonia had extended to the right lower lobe. In spite of another course of M. & B. 693, i.e. 84 tablets given as two tablets 4-hourly, the temperature continued to swing for eight days and the patient was desperately ill. After the eighth day the temperature settled, all his symptoms cleared and he made an uninterrupted recovery.

Discharged 24.3.39 after 47 days in hospital.

Up on 42nd day.



Name: Robert T.                      Case Letter: A 7.

Age: 46 years.                      Sex: Male.

Admitted 1.2.39.                      Day of illness: 2nd.

History: On day before admission felt shivery and "out of sorts"; later was seized by a sharp pain in the left side of chest, followed by a hard, painful cough, bringing up small quantities of reddish sticky sputum.

Examination of Chest: Dullness at left base and slightly impaired note below right clavicle. High pitched bronchial breathing at left base; diminished bronchial breath sounds at right upper lobe.

Cardio-Vascular System: Pulse bounding in character, with numerous extra-systoles; vessel wall palpable. Heart - apex beat in 6th space, outwith mid-clavicular line.

Sputum: Type II.



	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.4°F.	100	97.8
Pulse	132 p. min.	114	104
Respiration	52 p. min.	40	40
Blood Pressure	120/70		

White Blood Count: On admission, 24,000 per c.cm.  
7.2.39, 14,000 " "

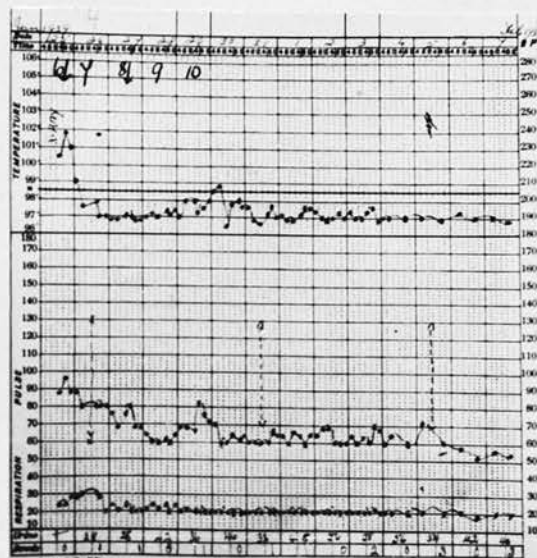
X-ray: 7.2.39 - Consolidation of right upper and left lower lobes.

M. & B. 693: Total dosage 28 tablets - 14 grms.  
Fall in temperature within 48 hours, i.e.  
after 16 tablets.

Complications: Hypertrophy and dilatation of heart.

Death 8.2.39.

Post-mortem: Double pneumonia, hypertrophy and dilatation of the heart, with an old-standing pericarditis.



Name: Angus MacD.      Case Letter: A 4.  
Age: 24 years.      Sex: Male.  
Admitted 25.1.39.      Day of illness: 5th.

History: Five days ago patient was seized by severe pain in left side of the chest, made worse by breathing and coughing.

Examination of Chest: Dullness on percussion over left infra-clavicular region; bronchial breath sounds; vocal fremitus and resonance increased.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.6°F.	97.8	97
Pulse	88 p. min.	80	80
Respiration	24 p. min.	30	20
Blood Pressure	130/62		

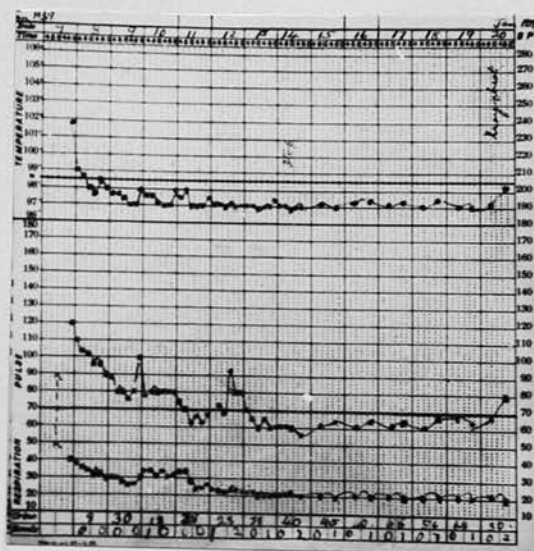
White Blood Count: On admission, 13,800 per c.cm.

X-ray: Consolidation of upper part of upper left lobe.

M. & B. 693: Total dosage - 28 tablets - 14 grms.  
Fall in temperature after 12 tablets, i.e.  
within 12 hours of admission.

Discharged 15.2.39 after 21 days in hospital.

Up on 12th day.



Name: Frank D.

Case Letter: F 2.

Age: 18 years.

Sex: Male.

Admitted 7.1.39.

Day of illness: 4th.

History: Four days ago patient developed pain in right side of chest; pain worse on coughing; sputum blood-stained.

Examination of Chest: Dullness of lower part of right lower lobe; high pitched bronchial breathing.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.8°F.	98	98
Pulse	120 p. min.	90	100
Respiration	40 p. min.	30	30
Blood Pressure	90/50		



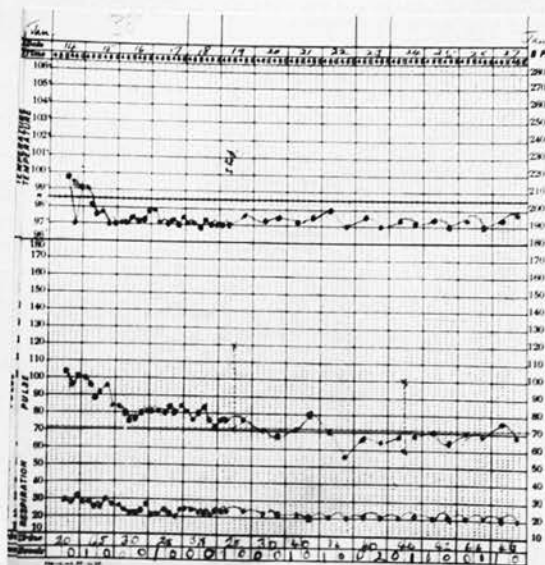
White Blood Count: On admission, 15,000 per c.cm.  
13.1.39, 5,400 " "

X-ray: 20.1.39 - Pneumonia not resolved.

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 10 tablets, i.e.  
in 12 hours.

Discharged 26.1.39 after 19 days in hospital.

Up on 16th day.



Name: Anthony G.      Case Letter: E 12.

Age: 37 years.      Sex: Male.

Admitted 14.1.39.      Day of illness: 2nd.

History: Two days before admission, shivering and vomiting; next day pain developed in right side of chest.

Examination of Chest: Dullness of right lower lobe;  
High pitched bronchial breathing.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100°F.	97.8	97.2
Pulse	104 p. min.	92	76
Respiration	30 p. min.	26	22
Blood Pressure	120/70		

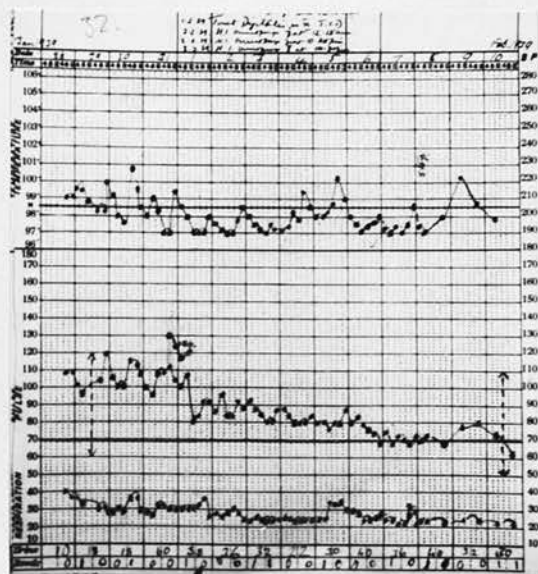
111.

White Blood Count:    On admission, 8000 per c.cm.  
                             19.1.39, 9,200 "    "  
                             14.2.39, 6,000 "    "

M. & B. 693:    Total dosage - 34 tablets - 17 grms.  
                             Fall in temperature after 12 tablets, i.e.  
                             within 24 hours.

Discharged 24.2.39 after 28 days in hospital.

Up on 18th day.



Name: Robert W. Case Letter: E 11.

Age: 66 years. Sex: Male.

Admitted 28.1.39. Day of illness: 4th.

History: Bronchitis all winter; pain in left side of chest for last three days.

Examination of Chest: Impairment of percussion note at left base; bronchial breathing and crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	99°F.	97	97
Pulse	110 p. min.	108	92
Respiration	40 p. min.	30	32
Blood Pressure	120/60		



White Blood Count: On admission, 31,000 per c.cm.  
13.2.39, 8,800 " "

X-ray: 6.3.39 - Unresolved pneumonia.

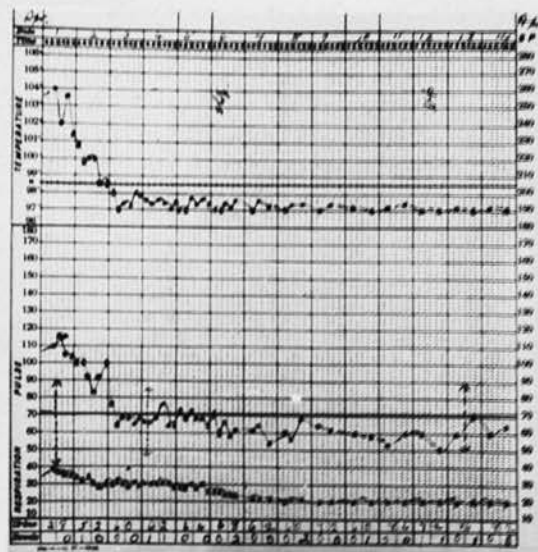
M. & B. 693: Total dosage - 36 tablets - 18 grms.  
Fall in temperature after 20 tablets.

Note: Treatment not started until two days  
after admission, when temperature  
rose to 101°F.

Complications: Extensive bronchitis and fibrosis;  
pneumonia still unresolved six weeks later.

Discharged 26.2.39 to Convalescent Home, after 29 days  
in hospital.

Up on 22nd day.



Name: John D.                      Case Letter: E 8.

Age: 16 years.                      Sex: Male.

Admitted 1.4.39.                      Day of illness: 4th.

History: Patient got wet at work, four days ago.  
Next day felt stiff and shivery and,  
twenty-four hours later, had a pain in  
his chest.

Examination of Chest: Some dullness at left base,  
with bronchial breath sounds.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	104°F.	100	97.4
Pulse	110 p. min.	100	68
Respiration	38 p. min.	32	32
Blood Pressure	90/40		

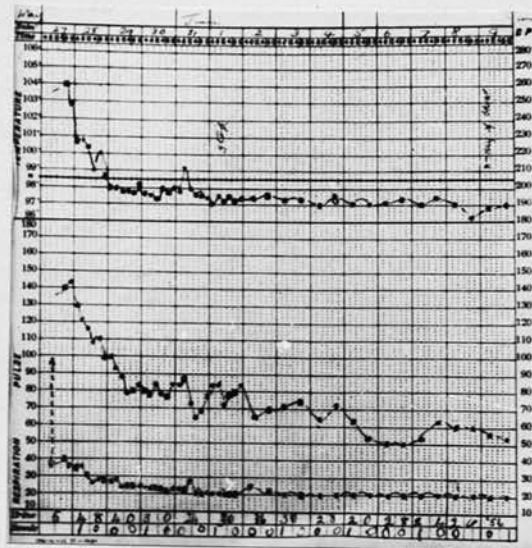
115.

White Blood Count: On admission, 13,800 per c.cm.  
4.4.39, 7,000 " "

M. & B. 693: Total dosage - 36 tablets - 18 grms.  
Fall in temperature after 20 tablets, i.e.  
within 36 hours.

Discharged on 17.4.39 to Convalescent Home, after  
16 days in hospital.

Up on 12th day.



Name: Andrew H.      Case Letter: E 6.

Age: 13½ years.      Sex: Male.

Admitted 27.5.39.      Day of illness: 2nd.

History: Patient felt ill while at school, yesterday.  
In the afternoon he had a pain in the  
right side of his chest.

Examination of Chest: Dullness in right axilla and  
upper part of right chest; friction-  
vesicular breathing.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	104°F.	100	97.8
Pulse	140 p. min.	110	80
Respiration	40 p. min.	28	24
Blood Pressure	98/38		



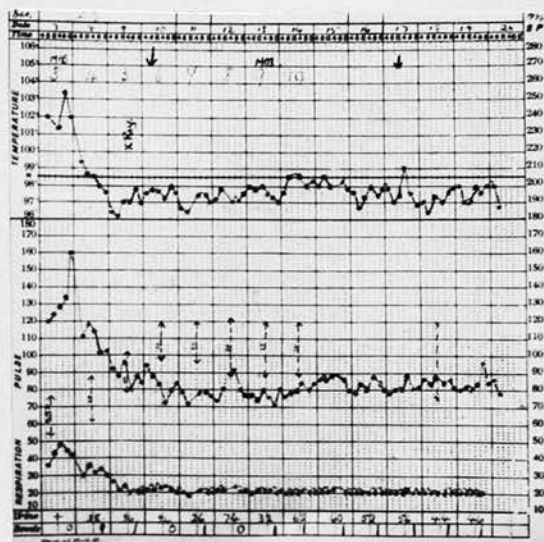
White Blood Count: On admission, 12,400 per c.cm.  
31.5.39, 8,200 " "

X-ray: 9.6.39 - Almost complete resolution.

M. & B. 693: Total dosage - 40 tablets - 20 grms.  
Fall in temperature after 14 tablets, i.e.  
within 24 hours.

Discharged 15.6.39, after 19 days in hospital.

Up on 17th day.



Name: John T.

Case Letter: D 9.

Age: 28 years.

Sex: Male.

Admitted 7.12.38.

Day of illness: 3rd.

History: Two days before admission patient had a shivering fit. This was followed by a sharp pain in the right side of the chest, aggravated by coughing and breathing.

Examination of Chest: Dullness at right base, with bronchial breathing; vocal fremitus and resonance showed marked increase.

Sputum: Type II.

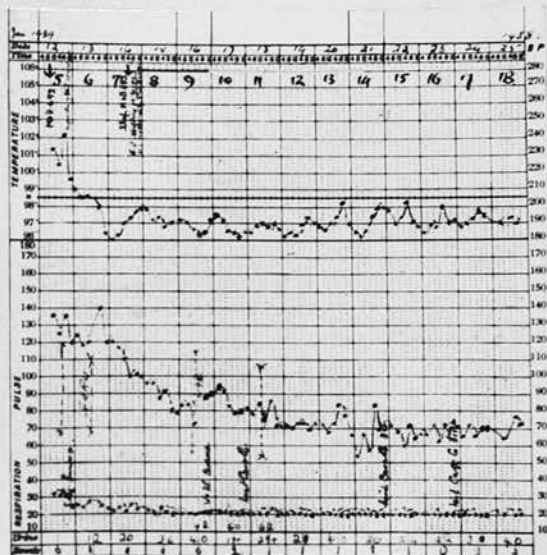
	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	99.4	96.2
Pulse	120 p. min.	110	88
Respiration	38 p. min.	30	20
Blood Pressure	78/52		

White Blood Count: On admission, 8,800 per c.cm.  
13.12.38, 6,700 " "

X-ray: Pneumonic consolidation of right lower lobe.  
17.1.39: Chest clear.

M. & B. 693: Total dosage - 30 tablets - 15 grms.  
Fall in temperature after 14 tablets i.e. 24  
hours later.

Discharged 20.12.38 after 14 days in hospital.



Name: Jessie R.

Case Letter: D 6.

Age: 16 years.

Sex: Female.

Admitted 12.1.39.

Day of illness: 4th.

History: Patient has had a cold for 14 days; four days ago had a pain in her chest.

Examination of Chest: Dullness of left base:  
bronchial breathing heard below angle of scapula.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.2°F.	98.4	97
Pulse	136 p. min.	120	110
Respiration	32 p. min.	28	22
Blood Pressure	120/68		

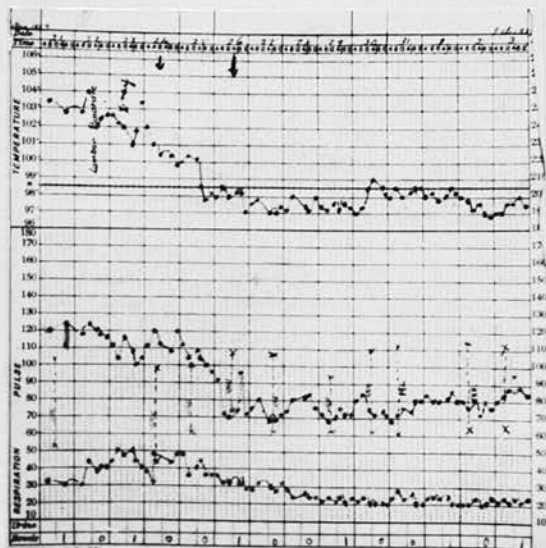


White Blood Count: On admission, 14,000 per c.cm.  
23.1.39, 10,800.

X-ray: Consolidation of left lower lobe.  
24.2.39 - Resolved.

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 12 tablets, i.e.  
24 hours after admission.

Discharged on 20.1.39 to Convalescent Home after 16  
days in hospital.



Name: Bernard McK.      Case Letter: D 4.

Age: 15 years.      Sex: Male.

Admitted 21.1.39.      Day of illness: 1st.

History: Feeling unwell for three days; pain started in back of right side of chest this morning.

Examination of Chest: Impaired percussion of right upper and middle lobes; harsh vesicular breathing with prolongation of expiration and a few fine crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103.2°F.	100.2	98.2
Pulse	120 p. min.	110	74
Respiration	32 p. min.	48	32
Blood Pressure	104/52		

White Blood Count: On admission, 20,000 per c.cm.  
3.2.39, 20,000 " "

X-ray: Consolidation of right upper, mid and lower lobes.

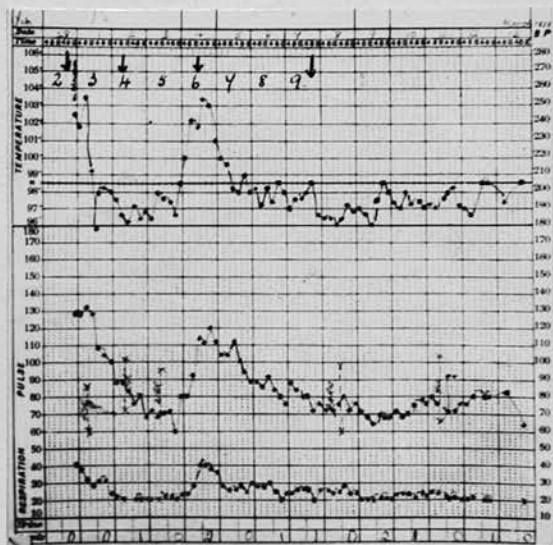
M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 18 tablets -  
though treatment not commenced till 4th day  
of illness.

Toxic Symptoms: Slight vomiting.

Complication: Boils on buttocks.

Discharged 28.2.39, after 38 days in hospital.

Up on 18th day.



Name: Charles A.

Case Letter: D 1.

Age: 22 years.

Sex: Male.

Admitted 28.2.39.

Day of illness: 2nd.

History: One night ago complained of shivering and this was followed shortly after by a pain in the left side of the chest, aggravated by coughing.

Examination of Chest: Vocal fremitus increased; dullness over left lower lobe; bronchial breath sounds; increased vocal resonance.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.4°F.	98	96.8
Pulse	130 p. min.	100	68
Respiration	40 p. min.	24	20
Blood Pressure	88/60		



White Blood Count: On admission, 24,600 per c.cm.  
6.3.39, 10,400 " "

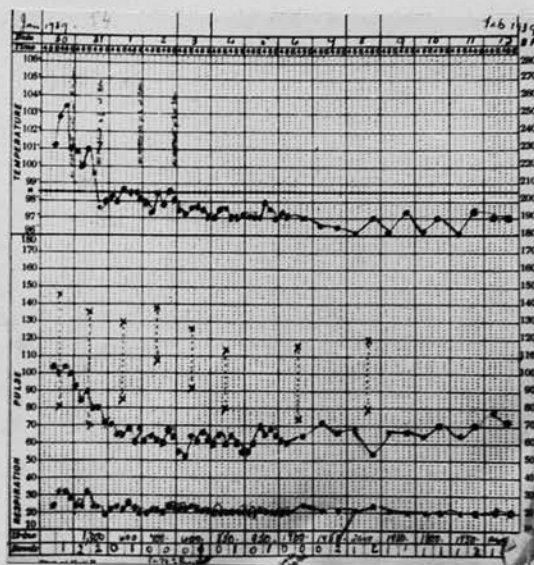
M. & B. 693: Total dosage - 22 tablets - 11 grms.  
Fall in temperature 12 hours after administration, i.e. 10 tablets.

Toxic Symptoms: Vomiting with stoppage of drug.

Complications: Temperature rose again on 6th day  
for twenty-four hours; M. & B. 693 resumed  
and continued till 7.3.39 - 40 tablets being  
given. Tendency to vomit remained.

Discharged on 13.3.39 after 13 days in hospital.

Up on 12th day.



Name: James B.

Case Letter: C 4.

Age: 23 years.

Sex: Male.

Admitted 30.1.39.

Day of illness: 2nd.

History: Pain in abdomen two days ago, followed by a cough next day.

Examination of Chest: Diminished expansion at right base with impaired percussion note and bronchial breathing.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.2°F.	101	98.6
Pulse	104 p. min.	90	64
Respiration	22 p. min.	32	22
Blood Pressure	142/80		

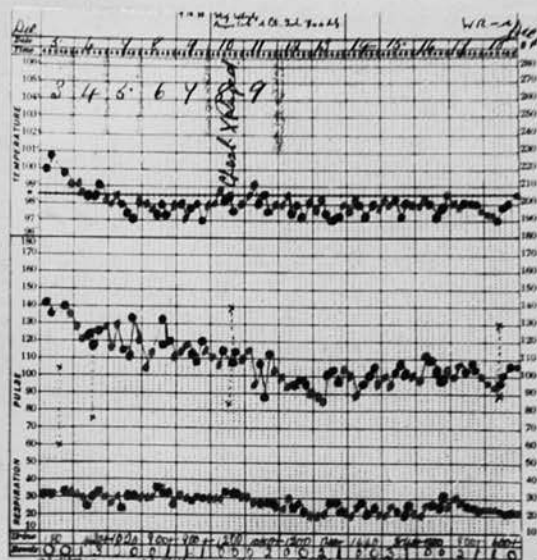
White Blood Count: On admission, 19,600 per c.cm.  
4.2.39, 8,600.

M. & B. 693: Total dosage - 30 tablets - 15 grms.  
Fall in temperature after 14 tablets, i.e.  
32 hours after treatment commenced.

Toxic Symptoms: Nausea and vomiting for two days.

Discharged on 25.2.39 after 25 days in hospital.

Up on 18th day.



Name: Mrs Jessie R.      Case Letter: C 7.

Age: 54 years.      Sex: Female.

Admitted 5.12.38.      Day of illness: 2nd.

History: Two days ago felt cold and shivery; next day had pain in right side of chest, associated with headache and vomiting. Later in the day patient collapsed.

Examination of Chest: Dull percussion note at right side of chest with bronchial breathing and fine crepitations at right base.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100°F.	99	98.4
Pulse	140 p. min.	128	108
Respiration	30 p. min.	30	28
Blood Pressure	104/60		



White Blood Count: On admission, 18,000 per c.cm.  
13.12.38, 11,200 " "

X-ray: Consolidation of right lower lobe with atelectasis of upper lobe.  
29.12.38: Resolving pneumonia.

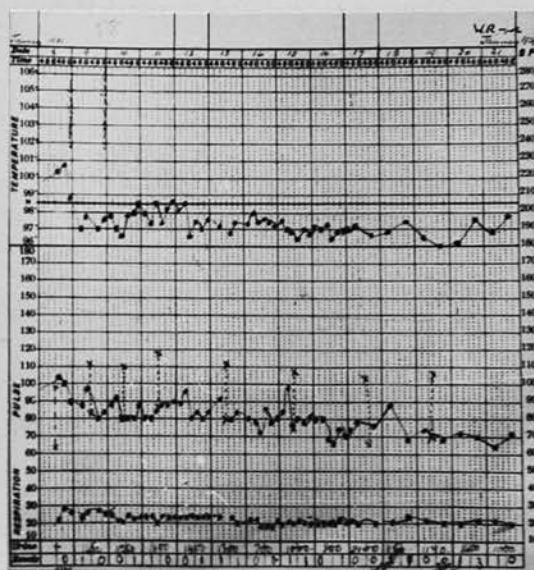
M. & B. 693: Total dosage - 36 tablets - 18 grms.  
Fall in temperature after 12 tablets, i.e.  
within 24 hours.

Toxic symptoms: Cyanosis.

Complications: Atelectasis of right upper lung lobe.

Discharged 7.1.39 after 34 days in hospital.

Up on 22nd day.



Name: George R.

Case Letter: C 8.

Age: 51 years.

Sex: Male.

Admitted 8.1.39.

Day of illness: 6th.

History: Not well since the New Year; four days ago loss of appetite and nausea; two days ago had a sharp pain in the left side - made worse on coughing.

Examination of Chest: Impaired movement at left base with impaired percussion note; also bronchial breathing with fine crepitations in this area.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.4°F.	97.4	97.8
Pulse	104 p. min.	90	80
Respiration	22 p. min.	28	24
Blood Pressure	98/64		

White Blood Count: On admission, 17,000 per c.cm.  
19.1.39, 8,800 " "

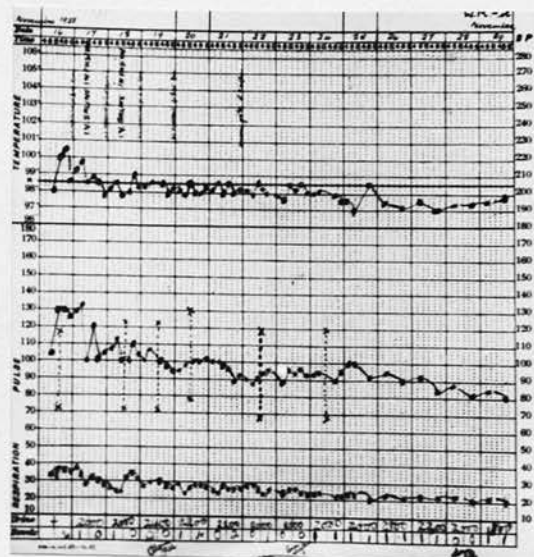
X-ray confirms consolidation.

M. & B. 693: Total dosage - 20 tablets - 10 grms.  
Fall in temperature after 10 tablets, i.e.  
in 20 hours.

Toxic Symptoms - Cyanosis: nausea.

Discharged on 7.2.39 to Convalescent Home after 30  
days in hospital.

Up on 22nd day.



Name: David B.

Case Letter: C 11.

Age: 62 years.

Sex: Male.

Admitted 16.11.38.

Day of illness: 4th.

History: Pain in right side of chest for four days, aggravated by work, and a cough which produced a white frothy spit.

Examination of Chest: Diminished movement on the right side, with dullness over the right base. Bronchial breathing accompanied by coarse crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100°F.	98.4	97.8
Pulse	130 p. min.	100	100
Respiration	38 p. min.	28	24
Blood Pressure	118/72		



White Blood Count: On admission, 11,000 per c.cm.  
22.11.38, 7,200 " "

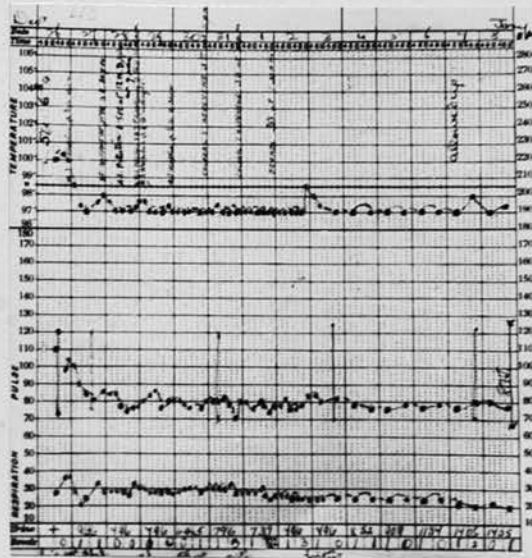
M. & B. 693: Total dosage - 23 tablets - 11.5 grms.  
Fall in temperature after 14 tablets.

Toxic Symptoms: Vomiting with stopping of M. & B.  
693.

Complications: Marked dehydration and extremely ill  
on admission, requiring two intravenous  
salines.

Discharged on 12.12.38 after a stay of 26 days.

Up on 16th day.



Name: Thomas G.                      Case Letter: H 15.

Age: 60 years.                      Sex: Male.

Admitted 26.12.38.                      Day of illness: 3rd.

History: Has had a cough for the past three weeks.  
Breathlessness since 24.12.38.

Examination of Chest: Diminished expansion of right side of chest; dullness of right middle and lower lobes; tubular breathing and increased vocal resonance.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100°F.	97.2	97
Pulse	110 p. min.	82	74
Respiration	28 p. min.	30	26
Blood Pressure	120/72		

135.

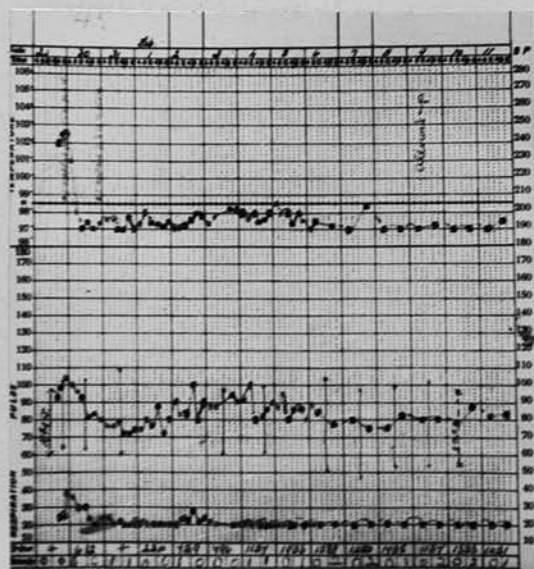
White Blood Count: On admission, 11,500 per c.cm.  
4.1.39, 12,000 " "

X-ray: 23.1.39 - Delayed resolution.  
13.2.39 - Still some obscurity.

M. & B. 693: Total dosage - 68 tablets - 34 grms.  
Fall in temperature after 10 tablets, i.e.  
within 24 hours.

Discharged 17.1.39 to Convalescent Home after 22 days  
in hospital.

Up on 13th day.



Name: Thomas A.

Case Letter: H 12.

Age: 15 years.

Sex: Male.

Admitted 29.1.39.

Day of illness: 3rd.

History: On 24.1.39 patient felt cold and shivery, had severe headache and felt sore all over. On 27.1.39 he developed pain in right side of chest.

Examination of Chest: Diminished expansion and dullness of right lower lobe; bronchial breathing and increased vocal resonance in this area.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	97	97.8
Pulse	94 p. min.	84	74
Respiration	24 p. min.	20	20
Blood Pressure	98/60		



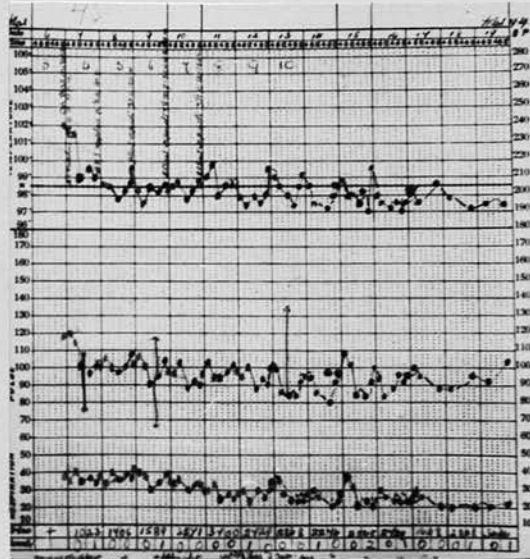
137.

White Blood Count: On admission, 10,000 per c.cm.  
10.2.39, 10,800.

M. & B. 693: Total dosage - 30 tablets - 15 grms.  
Fall in temperature after 12 tablets.

Discharged 23.2.39 after 25 days in hospital.

Up on 12th day.



Name: Charles S.

Case Letter: H 10.

Age: 24 years.

Sex: Female.

Admitted 6.3.39.

Day of illness: 3rd.

History: Off colour for about one week but continued work. On 7.3.39 had a shivering attack.

Examination of Chest: Diminished movement of left lower lobe; dullness in this area and bronchial breathing.

Sputum: Type II.

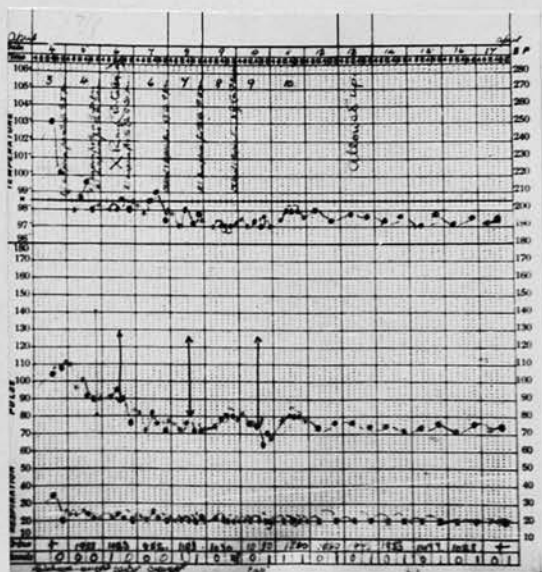
	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	99.4	99.6
Pulse	120 p. min.	100	102
Respiration	38 p. min.	38	42
Blood Pressure	108/74		

White Blood Count: On admission, 14,000 per c.cm.  
9.3.39, 14,000 " "

X-ray: 23.3.39 - Fluid at right base.

M. & B. 693: Total dosage - 72 tablets - 36 grms.  
Fall in temperature after 16 tablets, but  
continued rather irregular.

Complication: On 23.3.39 developed purulent fluid at  
right base, which necessitated surgical  
operation.



Name: John G.

Case Letter: G 6.

Age: 40 years.

Sex: Male.

Admitted 4.4.39.

Day of illness: 3rd.

History: Two days ago the patient had a violent shivering fit, followed by a sharp, stabbing pain between the shoulders.

Examination of Chest: Dullness of left upper lobe; breath sounds faint, with a few fine crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103°F.	99.4	98.6
Pulse	104 p. min.	100	90
Respiration	34 p. min.	24	22
Blood Pressure	140/80		



141.

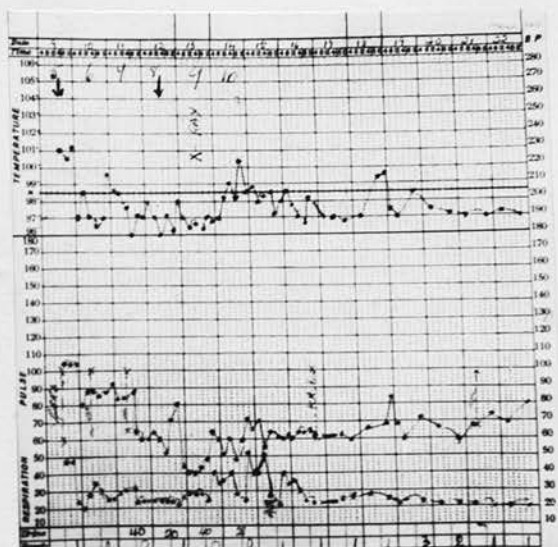
White Blood Count: On admission, 9,600 per c.cm.  
10.4.39, 9,000 " "

X-ray: Pneumonic consolidation of upper part of left lung field.

M. & B. 693: Total dosage - 62 tablets - 31 grms.  
Fall in temperature after 10 tablets.

Discharged 18.4.39 after 15 days in hospital.

Up on 10th day.



Name: Alexander B.      Case Letter: B 19.

Age: 29 years.      Sex: Male.

Admitted 9.3.39.      Day of illness: 5th.

History: Complained of feeling unwell five days ago; this was followed by a pain in the right side of his chest, aggravated by breathing and coughing.

Examination of Chest: Dullness of right lower lobe; absent breath sounds.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	96.4	96
Pulse	104 p. min.	86	60
Respiration	48 p. min.	30	24
Blood Pressure	100/60		

143.

White Blood Count: On admission, 20,400 per c.cm.  
20.3.39, 13,400 " "

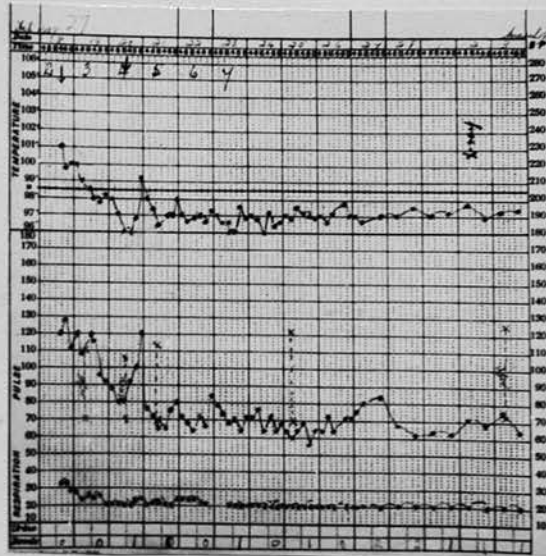
X-ray: 13.3.39 - Consolidation of right lung field.  
22.3.39 - Almost complete resolution.

M. & B. 693: Total dosage - 31 tablets - 15.5 grms.  
Fall in temperature 12 hours after admission,  
after 14 tablets.

Complications: Inter lobar empyaema developing on  
15.3.39: drained.

Discharged 28.3.39 to Convalescent Home.

Duration of stay in hospital: 20 days.



Name: John P.

Case Letter: B 16.

Age: 22 years.

Sex: Male.

Admitted: 18.2.39.

Day of illness: 2nd.

History: Patient well till yesterday morning, when he wakened at 5 a.m. complaining of pain all over his body; next he developed a severe pain in the left upper part of his chest.

Examination of Chest: Dullness over left lower lobe posteriorly, reaching to anterior axillary line; bronchial breathing, with harsh crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	98	96
Pulse	120 p. min.	114	92
Respiration	32 p. min.	24	20
Blood Pressure	110/70		



145.

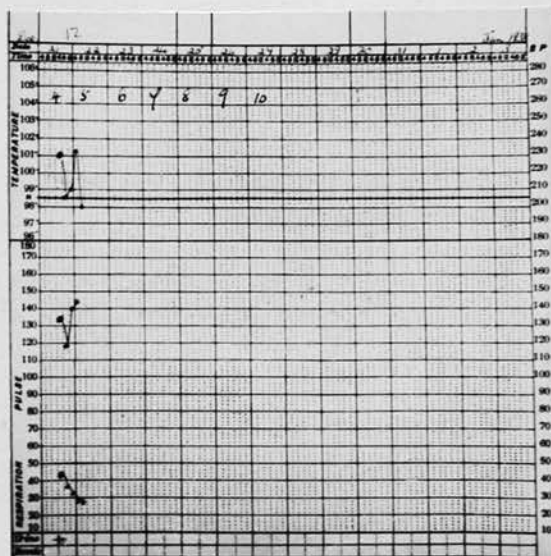
White Blood Count: On admission, 27,000 per c.cm.

X-ray: 2.3.39 - Negative.

M. & B. 693: Total dosage - 28 tablets - 14 grms.  
Fall in temperature after 16 tablets, i.e.  
within 24 hours.

Discharged 8.3.39 after 20 days in hospital.

Up on 17th day.



Name: Joshua L.

Case Letter: B 14.

Age: 43 years.

Sex: Male.

Admitted 21.12.38.

Day of illness: 4th.

History: Feeling ill for four days.

Examination of Chest: Large area of consolidation  
at right base; marked general bronchitis.

Sputum: Type II.

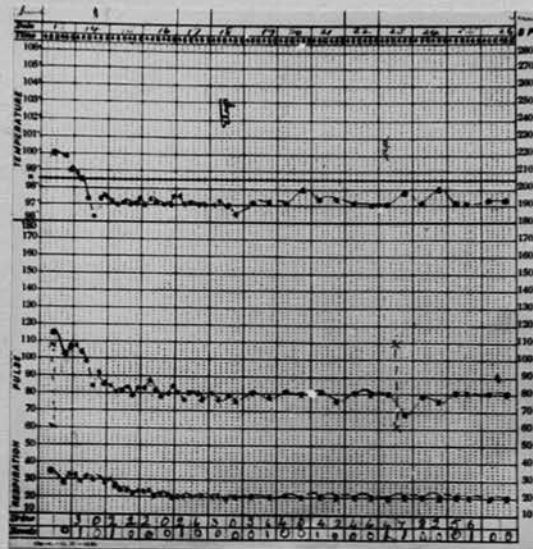
	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	101.2	
Pulse	134 p. min.	144	
Respiration	44 p. min.	28	
Blood Pressure	-		

147.

White Blood Count: On admission -

M. & B. 693: Total dosage - 12 tablets - 6 grms.

Summary: This patient died early the morning after admission, before the drug had time to become effective. He was very ill on admission, and also showed a marked general bronchitis.



Name: Charles H.

Case Letter: K 11.

Age: 16 years.

Sex: Male.

Admitted 13.6.39.

Day of illness: 2nd.

History: Vomiting two days ago; on day before admission, pain in the left iliac fossa.

Examination of Chest: Diminished expansion of left base; dullness of left base; breath sounds diminished, tubular in character.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100°F.	97.4	97
Pulse	114 p. min.	98	82
Respiration	34 p. min.	32	24
Blood Pressure	108/60		



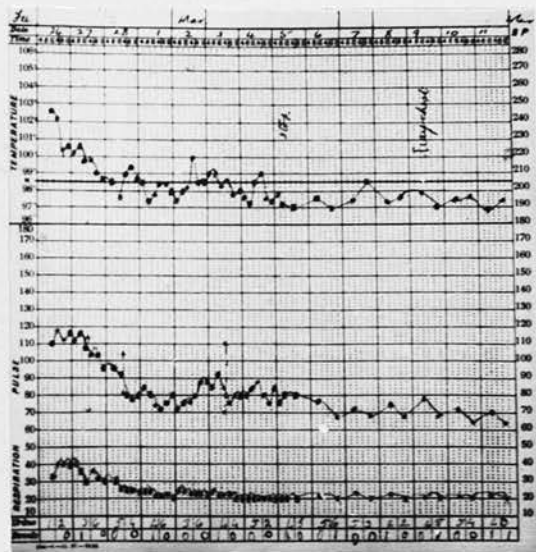
White Blood Count: On admission, 17,500 per c.cm.

X-ray: Inflammatory consolidation of left base.

M. & B. 693: Total dosage - 63 tablets - 31.5 grms.  
Fall in temperature after 8 tablets, i.e.  
20 hours.

Discharged 26.6.39 to Convalescent Home, after 14 days  
in hospital.

Up on 11th day.



Name: Thomas G.

Case Letter: K 9.

Age: 38 years.

Sex: Male.

Admitted 26.2.39.

Day of illness: 2nd.

History: Patient well till day before admission, when he had a sharp pain in the left side of the chest. A small amount of tenacious sputum.

Examination of Chest: Limited movement on left side; no impairment of percussion note. Vocal fremitus slightly increased over area the size of a five shilling piece round left nipple. Breath sounds harsh vesicular in that area, with coarse friction.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.6°F.	99.6	97.6
Pulse	110 p. min.	108	92
Respiration	32 p. min.	30	25
Blood Pressure	112/70		

151.

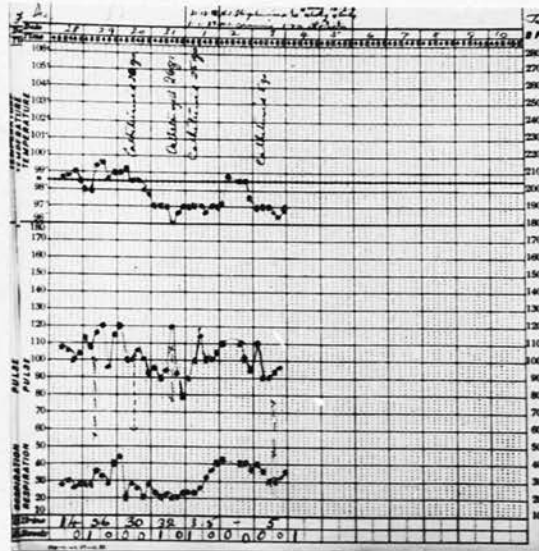
White Blood Count: On admission, 15,200 per c.cm.  
23.2.39, 11,000 " "

X-ray: Consolidation of left lung field.  
9.3.39 - Complete resolution.

M. & B. 693: Total dosage - 46 tablets - 23 grms.  
Fall in temperature after 20 tablets, i.e.  
36 hours.

Discharged 20.3.39 after 23 days in hospital.

Up on 15th day.



Name: Samuel B.

Case Letter: K 8.

Age: 63 years.

Sex: Male.

Admitted 27.12.38.

Day of illness: 4th.

History: Four days ago shivering and feeling ill.  
Pain developed in left side of chest that evening.

Examination of Chest: No movement on left side of chest, with marked dullness at base, absent breath sounds and friction sounds over cardiac apex.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	98.2°F.	99.4	98
Pulse	108 p. min.	116	100
Respiration	28 p. min.	36	28
Blood Pressure	100/56		



153.

White Blood Count: On admission, 9,500 per c.cm.  
31.12.38, 11,200 " "  
2.1.39, 9,100 " "

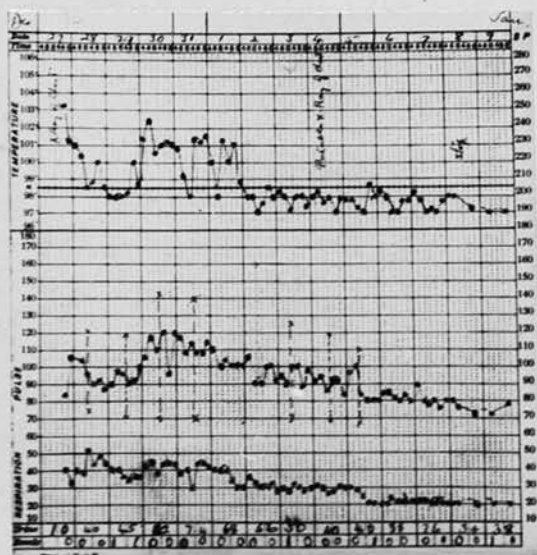
X-ray: Pneumonic consolidation of left lower lobe.

M. & B. 693: Total dosage - 58 tablets - 29 grms.  
Fall in temperature - irregular, never  
above 99.6°F.

Complication: Retention of urine.

Death: 3.1.39.

Summary: A thin, poorly nourished, toxic old man,  
with feeble pulse. No leucocytosis and  
no response to M. & B. 693.



Name: Arthur H.

Case Letter: K 7.

Age: 22 years.

Sex: Male.

Admitted 27.12.38.

Day of illness: 2nd.

History: Felt sick and shivery a week ago, and on day before admission had constant sharp pain in right side of chest.

Examination of Chest: Limitation of movement on right side; dullness over upper part of right side, anteriorly and posteriorly; high pitched bronchial breathing and a few fine crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103.2°F.	100	100
Pulse	82 p. min.	92	92
Respiration	40 p. min.	48	36
Blood Pressure	120/74		

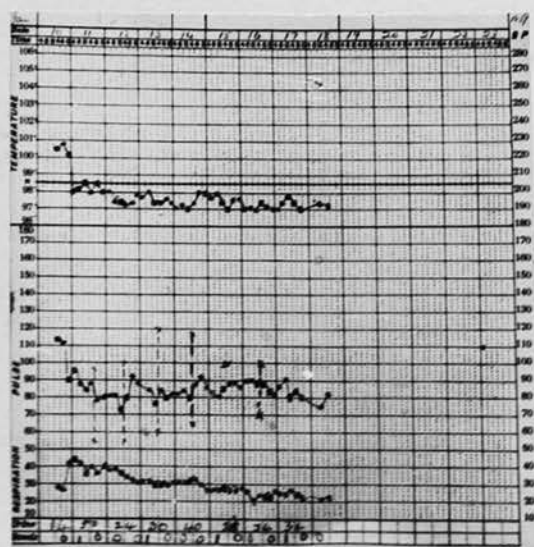
White Blood Count: On admission, 6,200 per c.cm.  
31.12.38, 41,800 " "  
5.1.39, 17,600 " "

X-ray: 28.12.38 - Pneumonic consolidation of right  
upper lobe.

M. & B. 693: Total dosage - 80 tablets - 40 grms.  
Fall in temperature after 18 tablets; rose  
again 24 hours later and continued for five  
days.

Discharged on 10.1.39 to Convalescent Home.

Duration of stay in hospital - 14 days.



Name: William McT.      Case Letter: K 6.

Age: 46 years.      Sex: Male.

Admitted 10.1.39.      Day of illness: 3rd.

History: Shivering attack six days before admission, and feeling unwell. Two days ago developed a bad pain in right side of chest.

Examination of Chest: Harsh vesicular breathing at right base, with crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.4°F.	98	97.2
Pulse	114 p. min.	88	80
Respiration	28 p. min.	40	34
Blood Pressure	96/54		

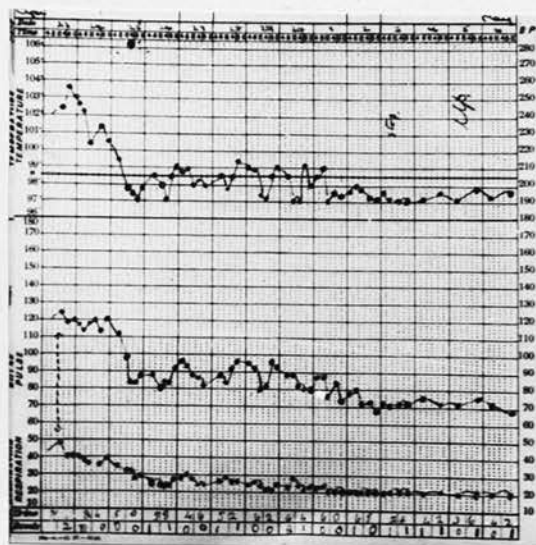


157.

White Blood Count: On admission, 11,000 per c.cm.  
16.1.39, 11,200 " "

M. & B. 693: Total dosage - 50 tablets - 25 grms.  
Fall in temperature after 10 tablets.

Discharged 18.1.39 to Convalescent Home after nine  
days in hospital: not up.



Name: George G.

Case Letter: K 3.

Age: 51 years.

Sex: Male.

Admitted 23.4.39.

Day of illness: 1st.

History: On day of admission patient developed a pain in the right side of the chest, with a cough which aggravated the pain.

Examination of Chest: Limited movement of right side; dullness on percussion and harsh vesicular breathing in the right lower lobe.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.4°F.	101	97.4
Pulse	124 p. min.	120	84
Respiration	48 p. min.	36	32
Blood Pressure	110/54		

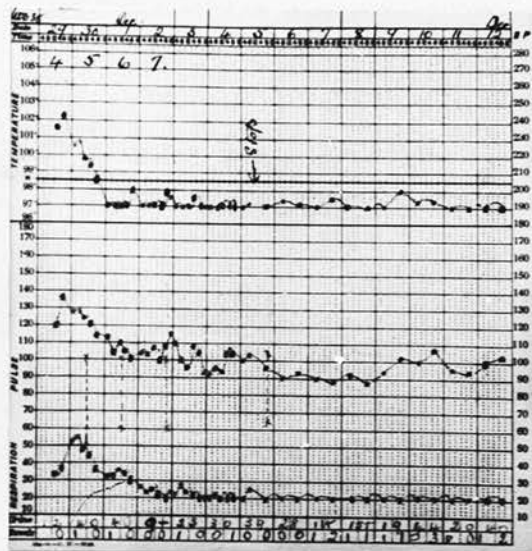
159.

White Blood Count: On admission, 17,600 per c.cm.

M. & B. 693: Total dosage - 60 tablets - 30 grms.  
Fall in temperature after 14 tablets, i.e.  
within 48 hours.

Discharged 8.5.39 after 16 days in hospital.

Up on 13th day.



Name: Mary B.

Case Letter: M 1.

Age: 13 years.

Sex: Female.

Admitted 29.11.38.

Day of illness: 4th.

History: Three days ago complained of a nagging pain in the right side; this became gradually worse, and hurt when she coughed. Cough was irritating and produced sputum tinged with dark blood.

Examination of Chest: Diminished movement right side of chest; impaired percussion note of right upper lobe, with high pitched bronchial breathing and increased vocal resonance, also many fine crepitations.

Sputum: Type II.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.6°F.	99.4	97
Pulse	120 p. min.	120	106
Respiration	32 p. min.	44	34
Blood Pressure	100/50		



161.

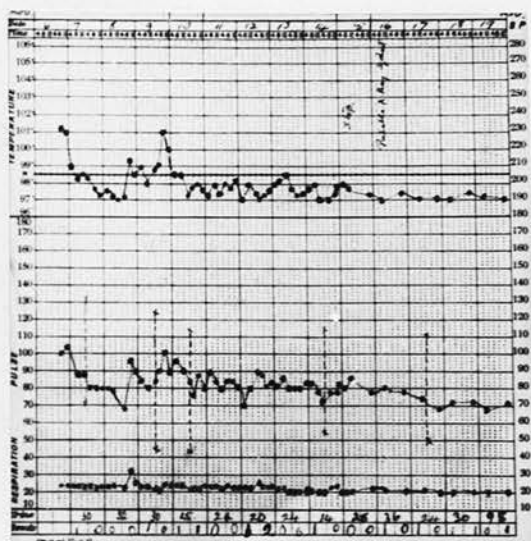
White Blood Count: On admission, 10,000 per c.cm.  
1.12.38, 12,400 " "  
5.12.38, 9,800 " "

X-ray: Pneumonic consolidation of right upper lobe.  
29.12.38 - Appearances normal.

M. & B. 693: Total dosage - 34 tablets.  
Fall in temperature after 8 tablets, i.e. 24  
hours later.

Discharged 3.12.38 after 34 days in hospital.

Up on 22nd day.



Name: Jessie B.

Case Letter: M 2.

Age: 17 years.

Sex: Female.

Admitted 6.11.38.

Day of illness: 5th.

History: Five days ago developed pains in the chest and shoulders, associated with a bad cough and copious sputum.

Examination of Chest: Dullness at left base; tubular breath sounds and a few fine crepitations in this region.

Sputum: Type II.

	On Admission	Treatment with M. & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.2°F.	97.6	99.4
Pulse	100 p.min.	80	96
Respiration	24 p.min.	24	32
Blood Pressure	132/70		

163.

White Blood Count: On admission, 14,600 per c.cm.  
13.11.38, 9,600.

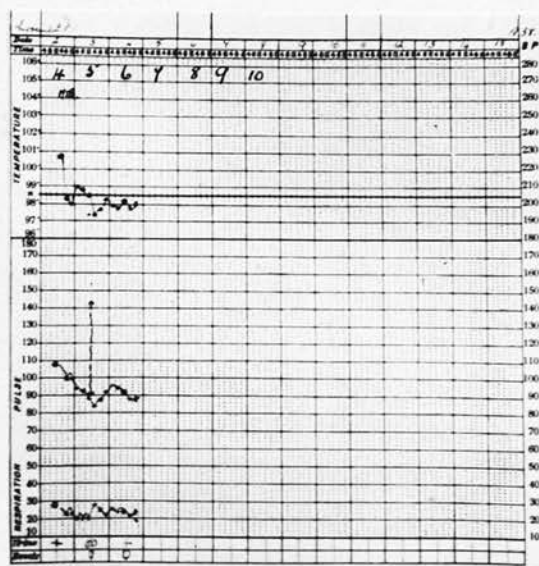
X-ray: 16.11.38 - Inflammatory process fast resolving.

M. & B. 693: Total dosage - 35 tablets - 17.5 grms.  
Fall in temperature after 8 tablets, i.e.  
within 12 hours of admission.

Complication: Temperature rose again to 101°F. 60  
hours later, but fell within 8 hours and  
continued normal.

Discharged on 24.11.38 to Convalescent Home after 18  
days in hospital.

Up on 16th day.



Name: George McL.

Case Letter: A 2.

Age: 67 years.

Sex: Male.

Admitted 2.11.38.

Day of Illness: 4th.

History: Patient had not been feeling well for four or five days. Three days before admission he had a sharp pain in the right side of his chest, aggravated by coughing.

Examination of Chest: Dullness of right upper lobe, with bronchial breathing and increased vocal fremitus and resonance.

Sputum: Type III.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.8°F.	97.4	98
Pulse	108 p. min.	88	88
Respiration	28 p. min.	28	24
Blood Pressure	140/90		



White Blood Count:    On admission, 14,000 per c.cm.  
                             4.11.38, 16,000    "    "

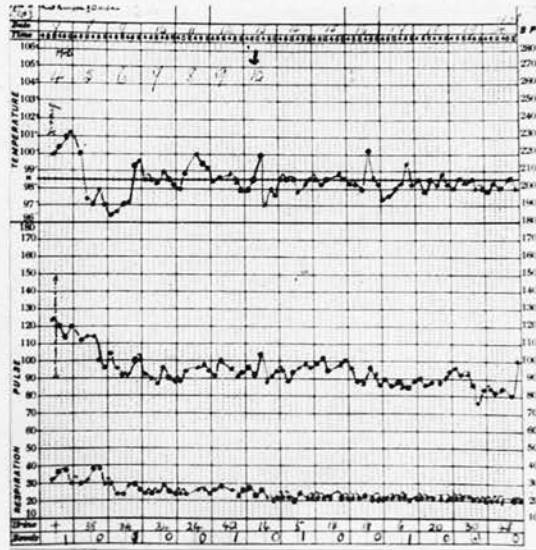
X-ray:    Consolidation of right upper lobe.

M. & B. 693:    Total dosage - 30 tablets - 15 grms.  
                             Fall in temperature after 8 tablets, i.e.  
                             within 12 hours.

Complication:    Delirium on second night after admis-  
                             sion, necessitating transfer to special ward.

Discharged 21.11.38 after 20 days in hospital.

Up on 7th day.



Name: Charles G.

Case Letter: A 3.

Age: 56 years.

Sex: Male.

Admitted 7.12.38.

Day of illness: 4th.

History: The patient has been troubled with a cough for three weeks before admission. Three days ago he had a shivering attack, followed by a sharp pain in the right side of the chest, aggravated by coughing and breathing.

Examination of Chest: Dullness at right base, with diminished breath sounds, bronchial in character.

Sputum: Type III.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100°F.	98	97.2
Pulse	124 p. min.	100	100
Respiration	32 p. min.	38	28
Blood Pressure	150/90		

167.

White Blood Count: On admission, 20,800 per c.cm.  
27.12.39, 13,000 " "

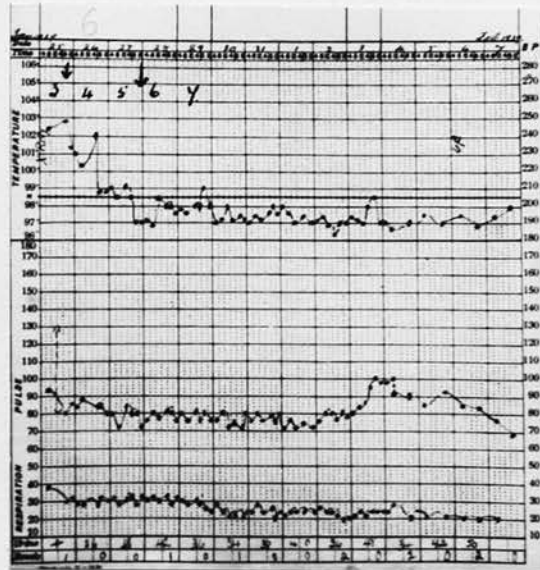
X-ray: Consolidation of right base.

M. & B. 693: Total dosage - 42 tablets - 21 grms.  
Fall in temperature after 14 tablets, but  
rose again.

Complication: Temperature rose again after 24 hours  
and continued for 14 days, off and on.

Discharged 19.1.39 after 45 days in hospital.

Up on 37th day.



Name: James D.                      Case Letter: A 6.

Age: 62 years.                      Sex: Male.

Admitted 25.1.39.                      Day of illness: 3rd.

History: Three days before admission patient felt very shivery and complained of pains all over body. On following day he developed a very painful cough, with dark red sputum.

Examination of Chest: Impaired movement of right upper chest with dull percussion note. Vocal fremitus and resonance increased; low-pitched bronchial breathing.

Sputum: Type III.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.4°F.	98.8	97
Pulse	92 p. min.	84	80
Respiration	38 p. min.	32	28
Blood Pressure	130/80		



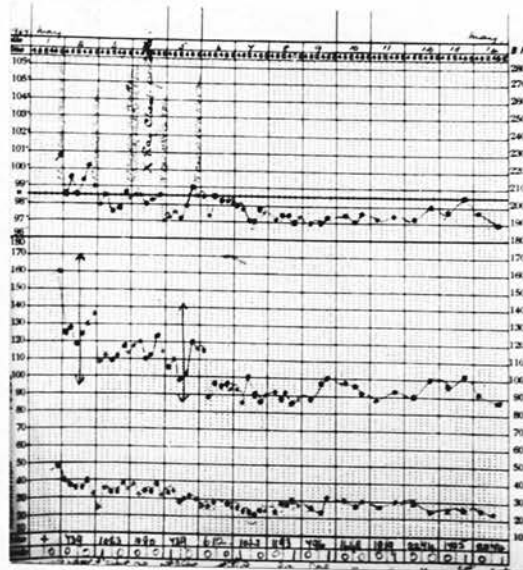
White Blood Count: On admission, 11,600 per c.cm.

X-ray: Consolidation of right upper lobe and a suggestion of fluid.  
9.2.39 - Inflammatory process has cleared considerably.

M. & B. 693: Total dosage - 36 tablets - 18 grms.  
Fall in temperature after 14 tablets, i.e.  
after 24 hours.

Discharged 15.2.39 after 21 days in hospital.

Up on 13th day.



Name: John M.

Case Letter: G 3.

Age: 63 years.

Sex: Male.

Admitted 1.5.39.

Day of illness: 6th.

History: Five days ago pain in the chest, and shivering.

Examination of Chest: Harsh vesicular breath sounds, coarse rhonchi and coarse friction sounds at left lower lobe.

Sputum: Type III.

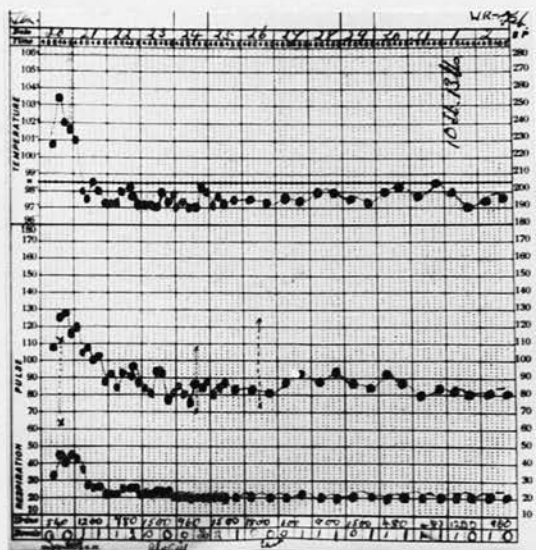
	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.8°F.	99	97
Pulse	160 p. min.	130	114
Respiration	50 p. min.	32	32
Blood Pressure	170/94		

White Blood Count: On admission, 9,600 per c.cm.  
4.5.39, 9,000 " "

X-ray: ? old inflammatory change in left lung.

M. & B. 693: Total dose - 49 tablets - 24.5 grms.  
Fall in temperature after 20 tablets, i.e.  
in 24 hours.

Discharged 27.5.39, after 26 days in hospital.



Name: Mrs Jean D.      Case Letter: C 12.

Age: 40 years.      Sex: Female.

Admitted 20.1.39.      Day of illness: 5th.

History: Pain in both sides of chest, with cough, for five days. On night before admission to hospital, pain localised to the left side.

Examination of Chest: Dullness at both bases, with diminished vesicular breath sounds and fine crepitations.

Sputum: Type III.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	98	97.2
Pulse	110 p. min.	104	84
Respiration	32 p. min.	36	22
Blood Pressure	110/62		



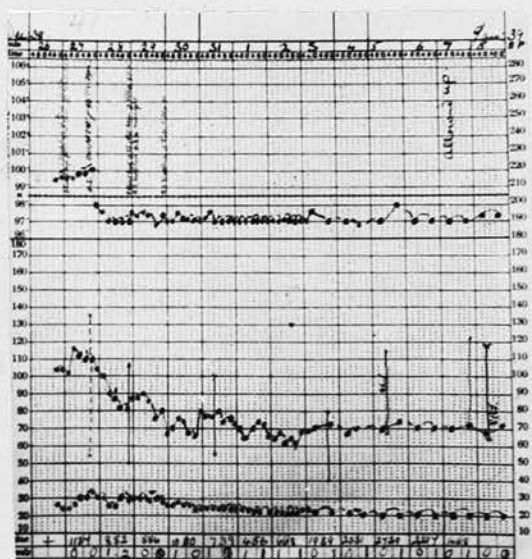
173.

White Blood Count: On admission, 11,000 per c.cm.  
28.1.39, 6,200.

M. & B. 693: Total dosage - 22 tablets - 11 grms.  
Fall in temperature after 10 tablets.

Discharged 8.2.39 after 19 days in hospital.

Up on 15th day.



Name: Leonard R.

Case Letter: H 14.

Age: 48 years.

Sex: Male.

Admitted 26.12.38.

Day of illness: 4th.

History: Been "of colour" for three weeks, with cold in head. On 23.12.38 developed pain in right side of chest, along with shivering attack.

Examination of Chest: Diminished expansion of right side; dullness on percussion of right upper and lower lobes; tubular breathing.

Sputum: Type III.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	99.4°F.	100	97
Pulse	104 p. min.	110	82
Respiration	28 p. min.	33	30
Blood Pressure	135/54		

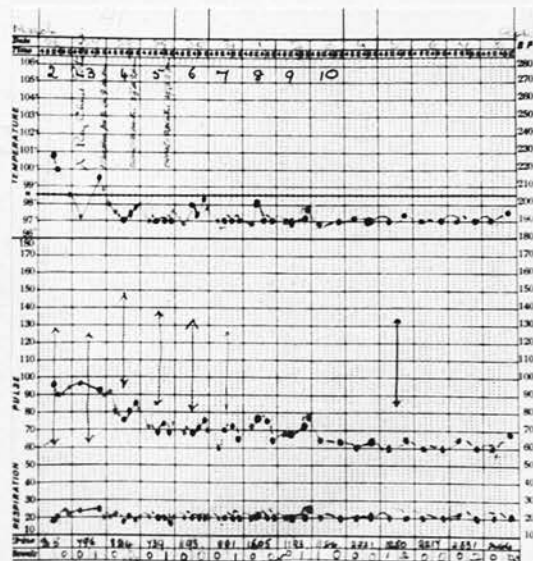
175.

White Blood Count: On admission, 12,200 per c.cm.  
4.1.39, 8,500 " "

M. & B. 693: Total dosage - 54 tablets - 27 grms.  
Fall in temperature after 16 tablets, i.e.  
in 26 hours.

Discharged 10.1.39 after 15 days in hospital.

Up on 13th day.



Name: Alexander McK.      Case Letter: G 8.

Age: 60 years.      Sex: Male.

Admitted 26.3.39.      Day of illness: 2nd.

History: Had a cold a week ago. On 25.3.39 he had a shivering fit and pain in the right side of the chest.

Examination of Chest: Diminished movement of right side; dullness and faint breath sounds.

Sputum: Type III.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.8°F.	98	97
Pulse	96 per min.	96	74
Respiration	20 per min.	24	22
Blood Pressure	128/62		



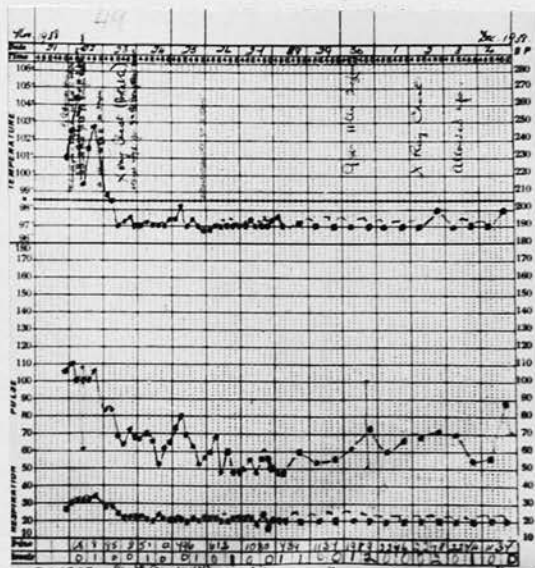
White Blood Count: On admission, 21,000 per c.cm.  
6.4.39, 8,400 " "

X-ray: Consolidation of right lower lung field.

M. & B. 693: Total dosage - 76 tablets - 38 grms.  
Fall in temperature after 20 tablets, i.e.  
in 24 hours.

Discharged 16.4.39 after 21 days in hospital.

Up on 15th day.



Name: James C. Case Letter: H 16.

Age: 26 years. Sex: Male.

Admitted 21.11.38. Day of illness: 4th.

History: Headache, cold and shivering on 16.11.38.  
Next morning had a sharp pain in the  
right side of his chest.

Examination of Chest: Diminished expansion right side  
of his chest; dullness of mid and lower  
lobes; breath sounds faint and friction  
over mid-lobe.

Sputum: Type 12 - mainly streptococcal.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	98.8	97
Pulse	108 p. min.	82	68
Respiration	28 p. min.	28	22
Blood Pressure	110/60		

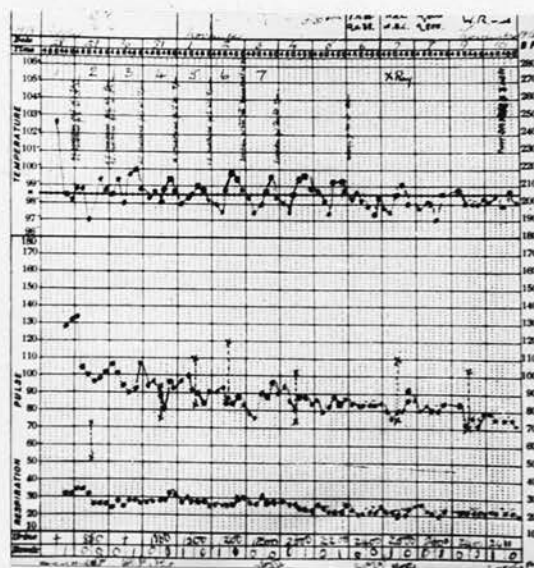
White Blood Count: On admission, 7,800 per c.cm.  
1.12.38, 5,200 " "

X-ray: 2.12.38 - Resolving pneumonia in mid-lobe.

M. & B. 693: Total dosage - 20 tablets - 10 grms.  
Fall in temperature after 8 tablets, i.e.  
within 24 hours.

Discharged 11.12.38 after 20 days in hospital.

Up on 13th day.



Name: Charles R.

Case Letter: C 3.

Age: 52 years.

Sex: Male.

Admitted 28.10.38.

Day of illness: 1st.

History: On the morning of admission to hospital had a severe shivering attack followed by an irritating cough and later a pain in his left side.

Examination of Chest: Impaired percussion note at left base, with diminished vesicular breath sounds and fine crepitations.

Sputum: Almost pure culture of haemolytic streptococci.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.6°F.	97	98
Pulse	128 p. min.	96	94
Respiration	32 p. min.	32	25
Blood Pressure	72/52		

White Blood Count: On admission, 18,000 per c.cm.  
9.11.38, 9,800 " "

X-ray: 7.10.39 - Pneumonic consolidation of left lung  
field.

M. & B. 693: Total dosage - 31 tablets - 15.5 grms.  
Fall in temperature after 4 tablets.

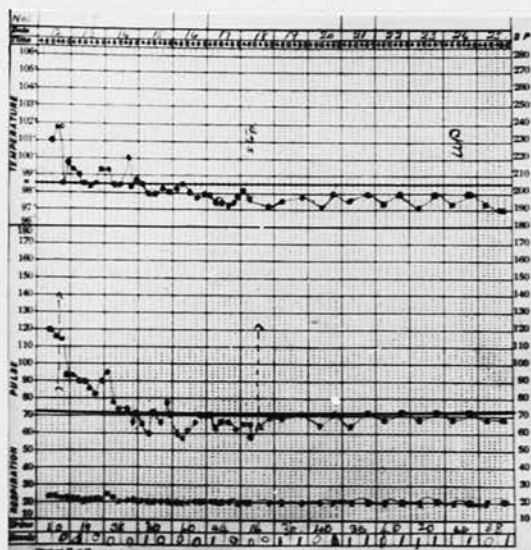
Toxic Symptoms: Slight nausea; cyanosis.

Complications: Carcinoma of penis - under treatment.

Discharged 14.11.38 to Convalescent Home.

Duration of stay in hospital: 17 days.





Name: Thady McN.

Case Letter: F 1.

Age: 19 years.

Sex: Male.

Admitted 12.11.38.

Day of illness: 3rd.

History: Two days ago patient had headache, nausea and vomiting. He then developed pain in the left side of his chest.

Examination of Chest: Dullness at left base: broncho-vesicular breath sounds with crepitations at the height of inspiration.

Sputum: Haemolytic streptococci.

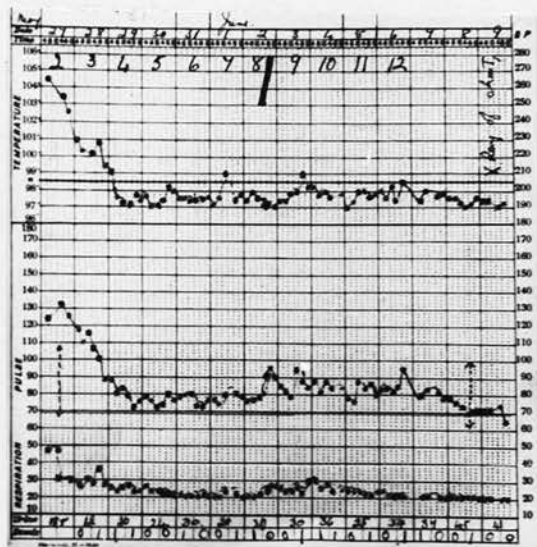
	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	98.4	98.4
Pulse	120 p. min.	90	74
Respiration	24 p. min.	20	20
Blood Pressure	140/84		

White Blood Count: On admission, 12,000 per c.cm.  
16.11.38, 8,200. " "

M. & B. 693: Total dosage - 44 tablets - 22 gms.  
Fall in temperature after 14 tablets i.e.  
in 24 hours.

Discharged on 28.11.38 to Convalescent Home after 17  
days in hospital.

Up on 13th day.



Name: Jeanette McD.

Case Letter: E 5.

Age: 30 years.

Sex: Female.

Admitted 27.5.39.

Day of illness: 2nd.

History: Felt well till yesterday when patient had a shivering fit and pain in the right side of chest.

Examination of Chest: Dullness at right base: some friction and bronchial breath sounds just audible.

Sputum: Non-haemolytic streptococci.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	104.5°F.	100.4	98
Pulse	124 p. min.	110	80
Respiration	48 p. min.	28	24
Blood Pressure	108/70		

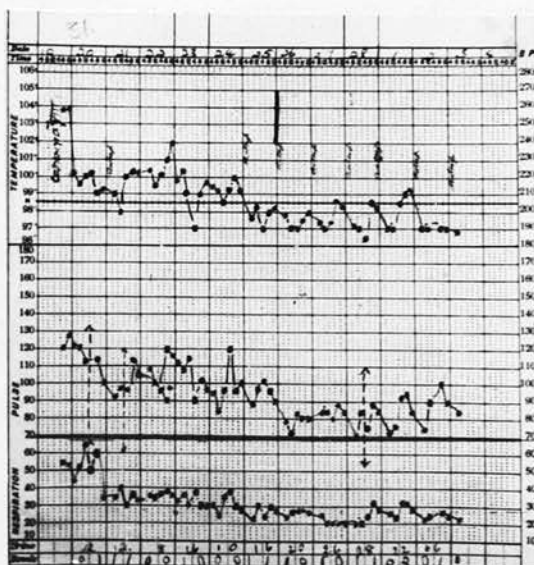
184.

White Blood Count: On admission, 13,000 per c.cm.  
3.6.39, 8,000. " "

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 20 tablets, i.e.  
36 hours after admission.

Discharged 22.6.39 after 26 days in hospital.

Up on 19th day.



Name: Mrs Jane S.

Case Letter: E 10.

Age: 26 years.

Sex: Female.

Admitted 14.2.39.

Day of illness: 1st.

History: Had influenza a week ago: this morning she developed a sharp pain in the region of the right breast, aggravated by breathing and coughing.

Examination of Chest: Dullness right lower lobe;  
patches of bronchial breathing.

Sputum: Non-haemolytic streptococci; some haemolytic streptococci; *M. catarrhalis* and staphylococci.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103.8°F.	99	100.4
Pulse	120 p. min.	114	114
Respiration	52 p. min.	60	36
Blood Pressure	130/70		



White Blood Count: On admission, 40,000 per c.cm.  
1.3.39, 12,000 " "

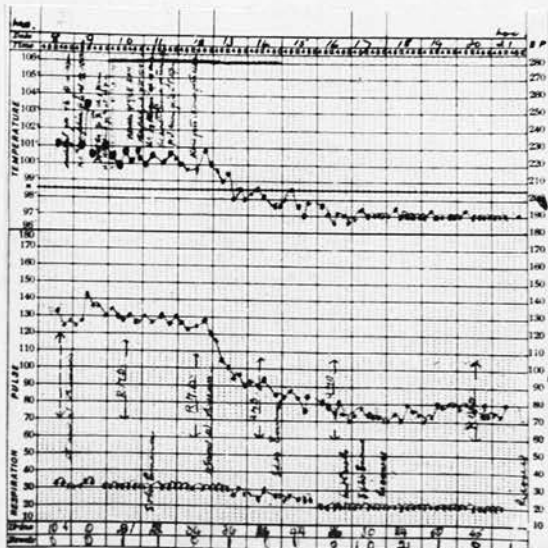
X-ray: 7.3.39 - Chest not clear.

M. & B. 693: Total dosage - 52 tablets - 26 grms.  
Fall in temperature - temperature did not  
fall till 25.2.39 and then tended to evening  
rise.

Toxic Symptoms: Cyanosis.

Discharged 3.3.39 to Convalescent Home.

Duration of stay in Hospital: 13 days.



Name: Catherine T.

Case Letter: D 7.

Age: 18 years.

Sex: Female.

Admitted 8.11.38.

Day of illness: 3rd.

History: Two days ago felt cold and shivery, and later on the same day developed pain in chest and cough.

Examination of chest: Dullness left base; vocal fremitus and resonance slightly increased; tubular breathing.

Sputum: Type 1 and 16.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101°F.	100	100.6
Pulse	132 p. min.	130	126
Respiration	32 p. min.	30	30
Blood Pressure	120/70		

188.

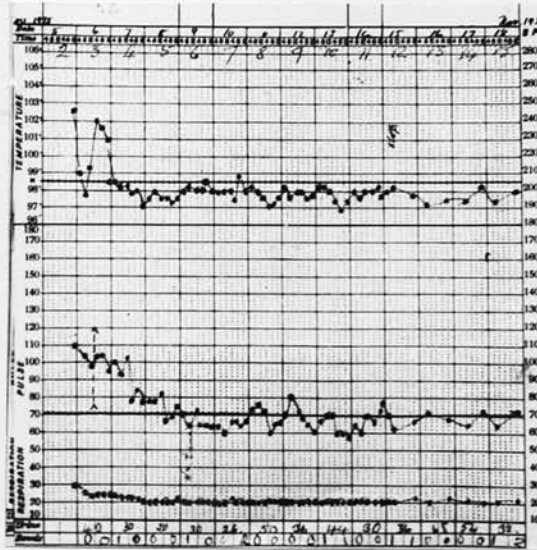
White Blood Count: On admission, 28,100 per c.cm.  
21.11.38, 9,600.

X-ray: Consolidation of left lower lobe.

M. & B. 693: Total dosage - 42 tablets - 21 grms.  
Fall in temperature after 42 tablets.

Discharged 2.12.38 to Convalescent Home after 24 days  
in hospital.

Up on 18th day.



Name: Joseph L.                      Case Letter: E 14.

Age: 17½ years.                      Sex: Male.

Admitted 5.11.38.                      Day of illness: 2nd.

History: Felt cold and shivery two days before admission; next morning had pains all over, with a sharp pain in the left side of the chest, worse on coughing and breathing.

Examination of Chest: Dullness at left base, with diminished breath sounds and friction rub.

Sputum: Type 1 and 6.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.8°F.	98.4	97.6
Pulse	110 p. min.	100	78
Respiration	30 p. min.	24	20
Blood Pressure	120/70		

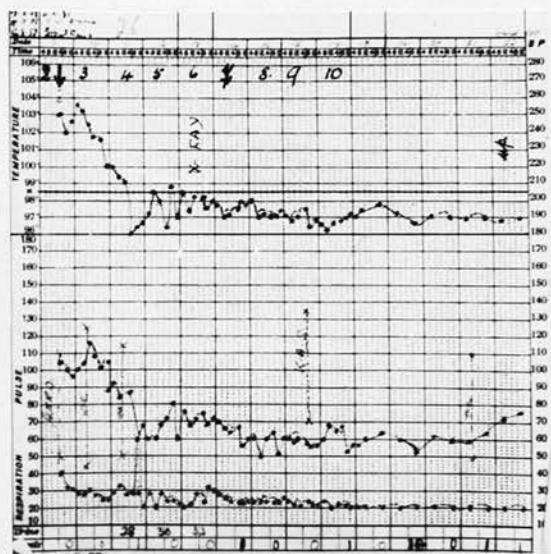
White Blood Count On admission, 11,000 per c.cm.  
14.11.38, 5,000.

X-ray: 28.11.38 - Complete resolution.

M. & B. 693: Total dosage - 30 tablets - 15 grms.  
Fall in temperature after 10 tablets, i.e.  
within 24 hours of treatment.

Discharged 22.11.38 to Convalescent Home after 17 days  
in hospital.





Name: James F.

Case Letter: B 15.

Age: 17 years.

Sex: Male.

Admitted 9.3.39.

Day of illness: 2nd.

History: Patient has not felt well for past few days; yesterday he had a severe pain in the chest, which was made worse by coughing and breathing.

Examination of Chest: Dullness of left lower lobe; vocal fremitus and resonance increased; bronchial breathing in upper part of left lower lobe.

Sputum: Types I and 18++.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103° F.	101.8	96
Pulse	108 p. min.	108	88
Respiration	40 p. min.	28	28
Blood Pressure	110/50		

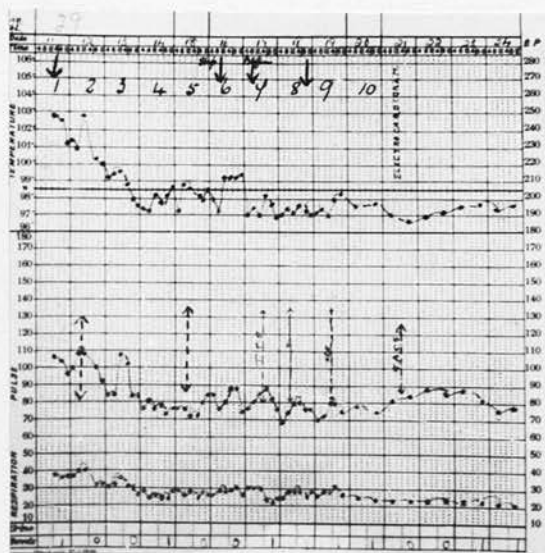
White Blood Count: On admission, 12,400 per c.cm.  
14.3.39, 16,400 " "

X-ray: Consolidation present in the middle of left lung field.

M. & B. 693: Total dosage - 60 tablets - 30 grms.  
Fall in temperature after 26 tablets, i.e.  
within 48 hours.

Discharged 28.3.39 to Convalescent Home after 20 days  
in hospital.

Up on 14th day.



Name: Arthur R.

Case Letter: B 18.

Age: 44 years.

Sex: Male.

Admitted 11.4.39.

Day of illness: 1st.

History: Patient awoke with a severe pain in the right side of chest on morning of admission; pain aggravated by breathing and coughing.

Examination of Chest: Dullness of right lower lobe; bronchial breath sounds; vocal fremitus and vocal resonance increased.

Sputum: Type 1++: Types 6, 20, and 22.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.8°F.	100.4	98.8
Pulse	108 p. min.	100	84
Respiration	38 p. min.	32	30
Blood Pressure	130/80		

White Blood Count: On admission, 7,200 per c.cm.  
21.4.39, 7,600 " "

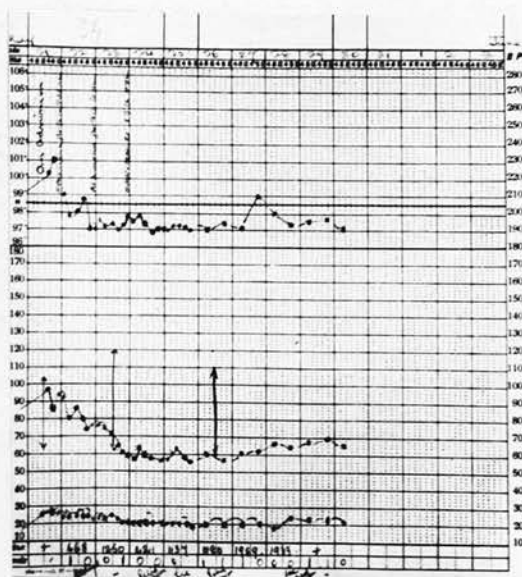
X-ray: 24.4.39 - No consolidation.

M. & B. 693: Total dosage 84 tablets - 42 grms.  
Fall in temperature after 30 tablets.

Toxic effects: Cyanosis.

Complication: Temperature rose to 99.2°F. on 6th day;  
M. & B. given for a further two days; no  
further temperature.

Discharged 25.4.39 to Convalescent Home after 14 days  
in hospital.



Name: Robert W.

Case Letter: G 1.

Age: 18 years.

Sex: Male.

Admitted 21.5.39.

Day of illness: 4th.

History: Four days ago patient had headache, nausea and vomiting. He could not sleep and was hot and restless. He has had some pain in left side of chest.

Examination of Chest: Dullness over left lower lobe; high pitched bronchial breathing, with fine crepitations at the height of inspiration.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.2°F.	98.8	97
Pulse	98 p. min.	80	66
Respiration	28 p. min.	24	22
Blood Pressure	102/62		

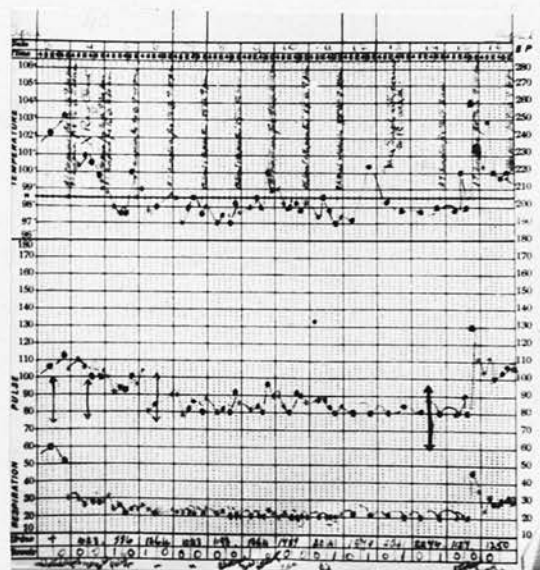


196.

White Blood Count: On admission, 12,000 per c.cm.

M. & B. 693: Total dosage - 36 tablets - 18 grms.  
Fall in temperature after 10 tablets, i.e.  
within 24 hours.

Discharged on 30.6.39 to Convalescent Home, after 10  
days in hospital.



Name: Robert B.

Case Letter: G 7.

Age: 43 years.

Sex: Male.

Admitted 3.4.39.

Day of illness: 2nd.

History: On Saturday (1.4.39) the patient had a shivering fit and the next day he had a sharp pain in the right side of his chest.

Examination of Chest: Restricted movement of right side; dullness over the right lower lobe; bronchial, high-pitched breath sounds; friction rub.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	101	97.6
Pulse	108 p. min.	106	94
Respiration	60 p. min.	26	26
Blood Pressure	100/74		

White Blood Count: On admission, 14,500 per c.cm.  
6.4.39, 8,800 " "

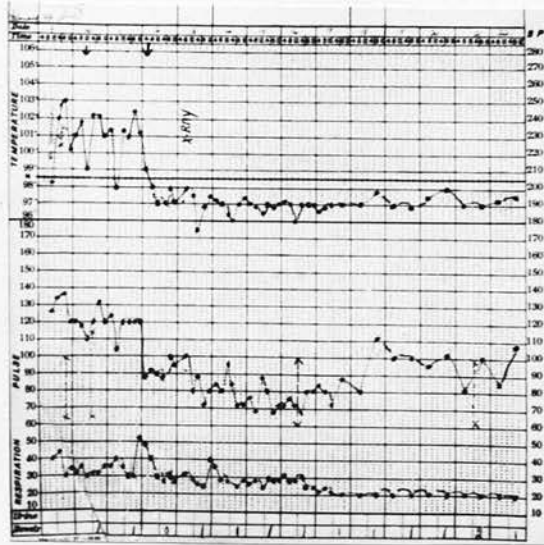
X-ray: 4.4.39 - Consolidation of right base.  
18.4.39 - Condition unchanged.

M. & B. 693: Total dosage - 65 tablets - 32.5 grms.  
Fall in temperature after 22 tablets.

Complications: Temperature rose slightly on the 9th and 12th days. On the 15th day it reached 104°F. and M. & B. 693 was again started - in all 41 tablets - and the temperature fell after 35 tablets. Temperature was due to marked axillary adenitis.

Discharged on 7.4.39 after 34 days in hospital.

Up on 28th day.



Name: Thomas McH.

Case Letter: B 17.

Age: 14 years.

Sex: Male.

Admitted 9.2.39.

Day of illness: 4th.

History: Cough and pain in the right side of the chest for three days.

Examination of Chest: Dullness of right lower lobe and increased vocal fremitus; harsh vesicular breath sounds; increased vocal resonance.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102°F.	99	101.4
Pulse	126 p. min.	110	120
Respiration	40 p. min.	30	35
Blood Pressure	98/62		

White Blood Count: On admission, 18,000 per c.cm.  
16.2.39, 9,100 " "

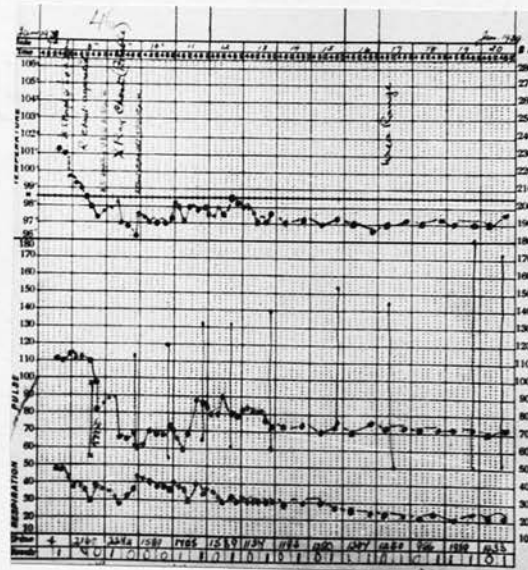
X-ray: 13.2.39 - Consolidation of right lower lobe.  
2.3.39 - Chest now almost clear.

M. & B. 693: Total dosage - 13 tablets - 6.5 grms.  
Fall in temperature after 13 tablets, i.e.  
7th day of illness.

Discharged 7.3.39 after 26 days in hospital.

Up on 16th day.





Name: Magnus R.

Case Letter: H 13.

Age: 19 years.

Sex: Male.

Admitted 7.1.39.

Day of illness: 4th.

History: On 4.1.39 patient developed pain in right side of chest, with headache, nausea and vomiting.

Examination of Chest: Diminished expansion of right side of chest; dullness of the right mid and lower lobes; absent breath sounds in mid and lower lobes.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.2°F.	98	96.8
Pulse	110 p. min.	110	66
Respiration	48 p. min.	30	32
Blood Pressure	98/54		

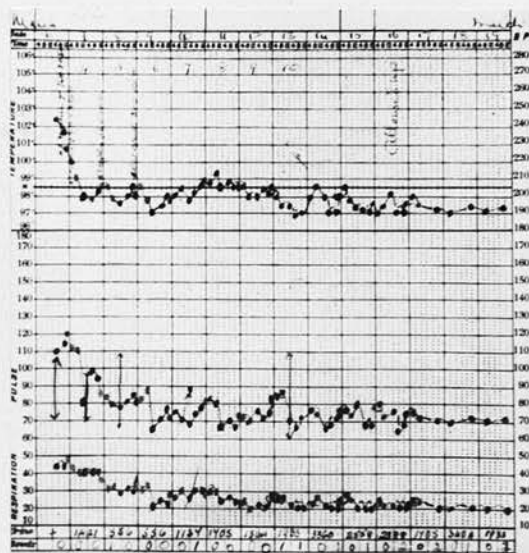
White Blood Count: On admission, 10,000 per c.cm.  
17.1.39, 6,300 " "

X-ray: Pneumonic consolidation of lower two-thirds of  
right lung field.  
6.2.39 - clear.

M. & B. 693: Total dosage - 39 tablets - 19.5 grms.  
Fall in temperature after 10 tablets.

Discharged on 31.1.39 to Convalescent Home after 24  
days in hospital.

Up on 15th day.



Name: Jacob M.

Case Letter: H 11.

Age: 15 years.

Sex: Male.

Admitted 6.3.39.

Day of illness: 3rd.

History: Well till evening of 4.3.39, when he felt cold and shivery, and had a pain in the right side of his chest.

Examination of Chest: Diminished movement on right side; dullness of right middle and lower lobes; tubular breathing.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.2°F.	97.8	98
Pulse	110 p. min.	98	81
Respiration	42 p. min.	40	30
Blood Pressure	104/70		

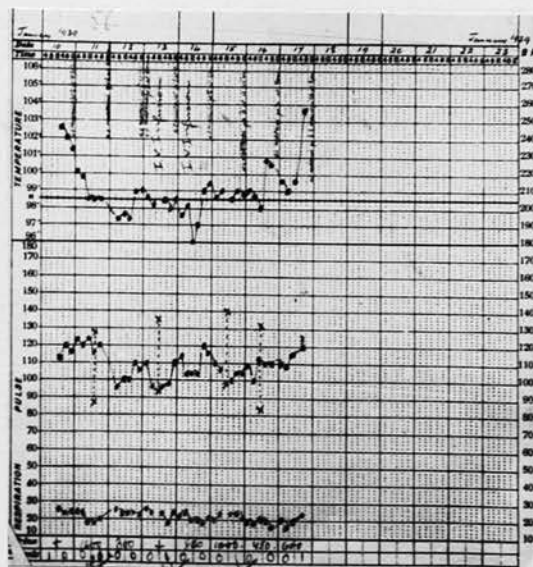
204.

White Blood Count: On admission, 20,200 per c.cm.  
9.3.39, 19,400 " "

M. & B. 693: Total dose - 78 tablets - 39 grms.  
Fall in temperature in 12 hours, i.e. after  
10 tablets.

Discharged on 27.3.39 after 21 days stay in hospital.

Up on 11th day.



Name: Joseph P.

Case Letter: C 6.

Age: 61 years.

Sex: Male.

Admitted 11.1.39.

Day of illness: 2nd.

History: Pain behind the right shoulder for two days;  
cough for four months; swelling in the  
throat being treated by X-ray.

Examination of Chest: Diminished movement and dullness  
at right base; breath sounds obscured by  
pleural friction.

Sputum: No organisms.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	102.6°F.	98.4	97.2
Pulse	114 p. min.	116	100
Respiration	26 p. min.	18	24
Blood Pressure	128/86		



White Blood Count: On admission, 15,800 per c.cm.  
13.1.39, 11,800 " "  
15.1.39, 16,600 " "

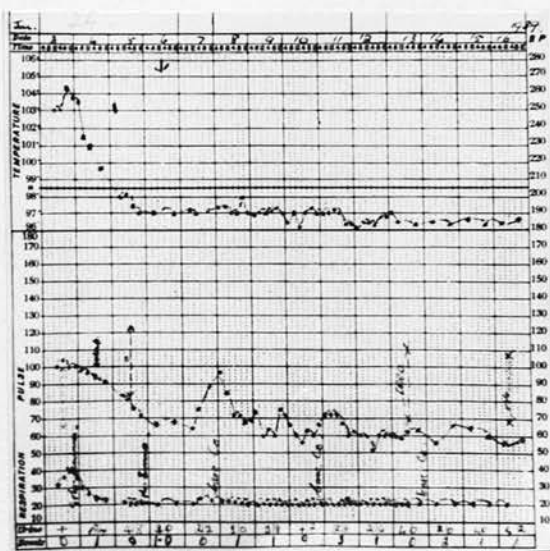
X-ray: Opacity of the lower part of the right lung field.

M. & B. 693: Total dosage - 24 tablets - 12 grms.  
Temperature fell after 12 tablets, i.e. 16 hours after admission.

Complications: Carcinoma of the pharynx with extensive secondaries of the liver and associated lymph glands.

Death 17.1.39.

Post-mortem: Carcinoma of pharynx; secondaries of liver and glands. Patchy consolidation of the right lower lung.



Name: Mrs Ellen W.

Case Letter: D 10.

Age: 56 years.

Sex: Female.

Admitted 3.1.39.

Day of illness: 1st.

History: Patient had not felt well for one week before admission. She had a cold, accompanied by some cough. On day of admission she woke with pain in right side, and shivering attack.

Examination of Chest: Dullness on percussion at right base; hoarse vesicular breathing and increased vocal resonance.

Sputum: None.

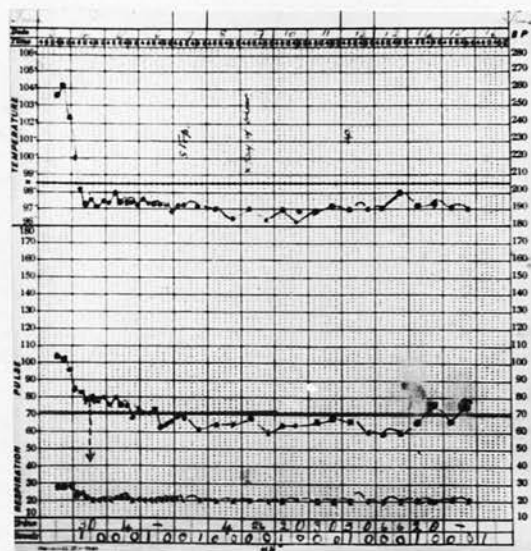
	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103°F.	98	97
Pulse	100 p. min.	84	66
Respiration	32 p. min.	22	20
Blood Pressure	104/68		

White Blood Count: On admission, 14,000 per c.cm.

M. & B. 693: Total dosage, 32 tablets - 16 grms.  
Fall of temperature after 12 tablets, i.e.  
within 24 hours.

Discharged on 21.1.39, after 19 days in hospital.

Up on 15th day.



Name: James G.

Case Letter: E 4.

Age: 21 years.

Sex: Male.

Admitted 3.6.39.

Day of illness: 2nd.

History: Had a cold for about a week; pain in right side of chest for one day, worse on coughing.

Examination of Chest: Impaired percussion note; faint breath sounds; increased vocal resonance.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103.8°F.	97.4	97.4
Pulse	104 p. min.	80	74
Respiration	28 p. min.	20	20
Blood Pressure	80/42		

210.

White Blood Count: On admission, 8,400 per c.cm.  
6.6.39, 8,000 " "

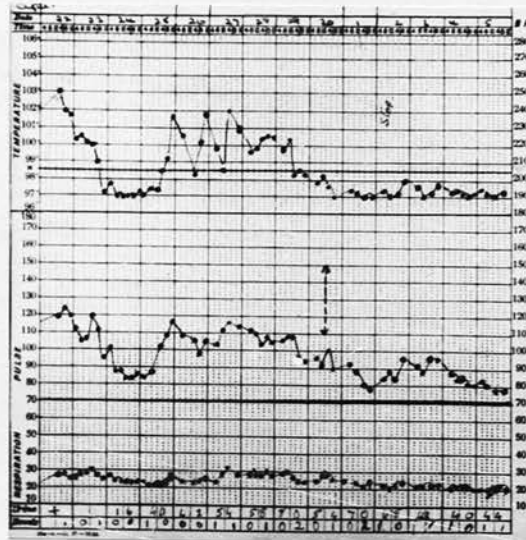
X-ray: 12.6.39 - No consolidation; some increased  
density of right base.

M. & B. 693: Total dosage - 26 tablets - 13 grms.  
Fall in temperature after 10 tablets.

Discharged on 15.6.39 to Convalescent Home after 13  
days in hospital.

Up on 10th day.





Name: Andrew G.

Case Letter: E 7.

Age: 46 years.

Sex: Male.

Admitted 22.4.39.

Day of illness: 2nd.

History: Pain in chest for one day; had a shivering fit on day before admission, and then later had pain in left side of chest.

Examination of Chest: Dullness of left lower lobe, with bronchial breathing.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	103°F.	100	97
Pulse	120 p. min.	120	84
Respiration	28 p. min.	30	24
Blood Pressure	150/110		

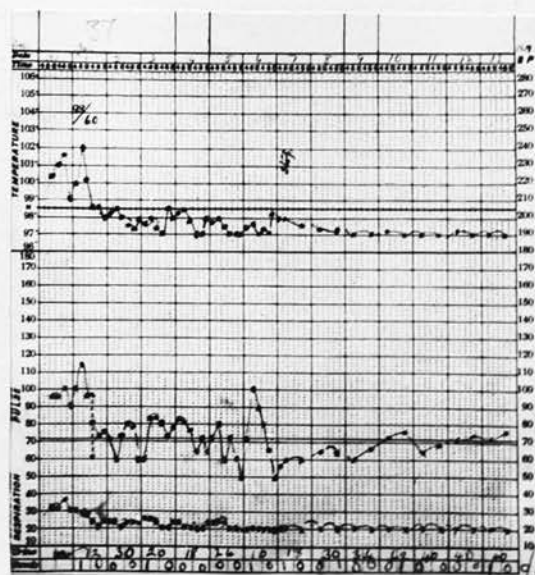
White Blood Count: On admission, 7,500 per c.cm.  
27.4.39, 23,600 " "  
2.5.39, 11,200 " "

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 18 tablets.

Complications: Temperature rose again on 25.4.39,  
i.e. 5th day of illness; 28 tablets of  
M. & B. 693 were given, with no effect, and  
the temperature fell after five days.

Discharged on 18.5.39 after 26 days in hospital.

Up on 18th day.



Name: Robert B.

Case Number: E 13.

Age: 12 years.

Sex: Male.

Admitted 31.12.38.

Day of illness: 3rd.

History: Shivering and vomiting three days ago,  
followed by pain in left side of chest.

Examination of Chest: Dullness of left lower lobe;  
high pitched bronchial breathing.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.2°F.	100.2	98
Pulse	98 p. min.	96	74
Respiration	30 p. min.	28	20
Blood Pressure	98/60		

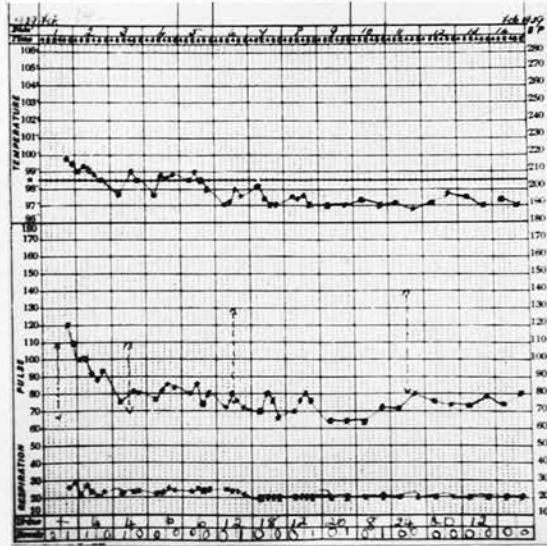
214.

White Blood Count: On admission, 17,000 per c.cm.  
4.1.39, 7,200 " "

M. & B. 693: Total dosage - 32 tablets - 16 grms.  
Fall in temperature after 16 tablets.

Toxic Symptoms: Vomiting on 4th day of treatment.

Discharged on 13.1.39 after 14 days in hospital.



Name: Mrs Mary L.

Case Number: A 11.

Age: 66 years.

Sex: Female.

Admitted 1.2.39.

Day of illness: 3rd.

History: Had been in bed for three weeks, due to poor health; then, two days before admission, was troubled by pain in the left side of the chest, which was aggravated by coughing.

Examination of Chest: Impaired movement on left side, with dullness at base; bronchial breathing with occasional crepitations.

Sputum: None.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	99.8°F.	98.4	98.4
Pulse	120 p. min.	92	80
Respiration	30 p. min.	24	24
Blood Pressure	110/65		

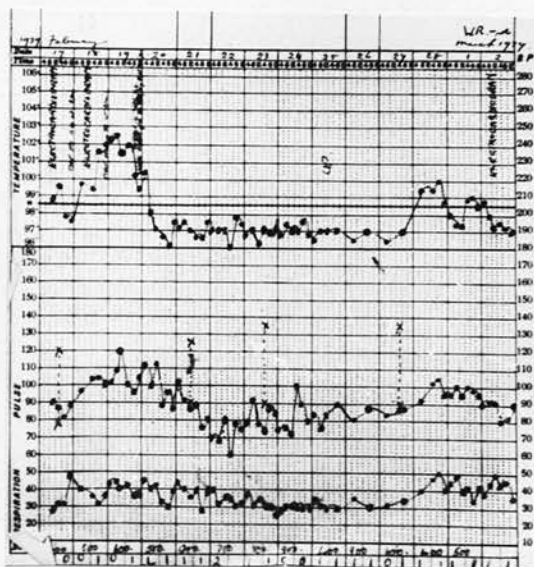


White Blood Count: On admission, 14,000 per c.cm.

M. & B. 693: Total dosage - 28 tablets.  
Fall in temperature after 10 tablets.

Discharged on 22.2.39 after 21 days in hospital.

Up on 16th day.



Name: Lindsay R.

Case Letter: M 3.

Age: 81 years.

Sex: Male.

Admitted 17.2.39.

Day of illness: 1st.

History: Not so well for some time past; had to go shopping for groceries - collapsed and brought to hospital.

Examination of Chest: Increased dullness of left side of chest; fine crepitations.

Sputum: Not typed.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	101.6°F.	96	96.6
Pulse	104 p. min.	96	76
Respiration	40 p. min.	30	28
Blood Pressure	122/85		

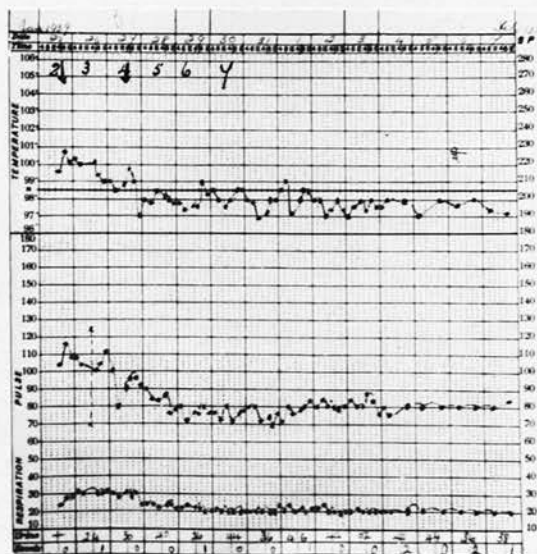
White Blood Count: On admission, 7,400 per c.cm.  
21.2.39, 9,600 " "

M. & B. 693: Total dosage - 19 tablets - 9.5 gm.  
Fall in temperature after 8 tablets, i.e.  
9 hours after administration.

Complication: Admitted as a case of auricular fibril-  
lation with right bundle-branch block;  
myocardial degeneration and coronary infarct.  
Pneumonia did not set in till third day in  
hospital, and was regarded as terminal.

Discharged 27.3.39 to Hospital for Chronic Illnesses,  
after 38 days in hospital.

Up on 7th day.



Name: Robert D.

Case Letter: A 5.

Age: 35 years.

Sex: Male.

Admitted 25.1.39.

Day of illness: 2nd.

History: Patient left hospital after operation for inguinal hernia five days ago. Yesterday he had an attack of shivering, followed by a sharp pain in the right side of the chest.

Examination of Chest: Diminished movement and impaired note at right base; bronchial breathing.

Sputum: No reaction to any type.

	On Admission	Treatment with M & B 693	
		After 24 hrs.	After 48 hrs.
Temperature	100.8°F.	99.4	99
Pulse	116 p. min.	104	96
Respiration	30 p. min.	30	30
Blood Pressure	125/70		

White Blood Count: On admission, 14,200 per c.cm.

M. & B. 693: Total dosage - 30 tablets - 15 grms.  
Fall in temperature after 24 tablets - slow  
response.

Discharged 18.2.39 after 24 days in hospital.

Up on 13th day.



DISCUSSION.

It is at this stage that it becomes necessary to marshall the facts which will help us to give an answer to the various questions which we have set ourselves to answer.

Eighty-five cases of Lobar Pneumonia have been treated with 2-sulphanilyl-aminopyridine, or M. & B. 693, and the important features of each have been set out in the previous section. What information, then, has been acquired in treating these cases? Has the discovery of M. & B. 693 brought us nearer to a solution of the problem of the treatment of Pneumonia? At the outset I realise that the number of cases treated is comparatively small and that, in consequence, no final opinion can be given from their survey. It is possible, however, to draw certain conclusions and these, with the results of other observers, may serve to add something to the assessment of this drug M. & B. 693.

What effect, then, does treatment with M. & B. 693 have on the course of a case of pneumonia? Has it any striking action on the disease? To this question the answer is undoubtedly 'yes'. In the

majority of cases there is a dramatic effect within a short period of the initial administration of the drug. In an interval varying from twenty-four to thirty-six hours, and in most cases within the twenty-four hours after giving M. & B. 693, the temperature falls abruptly and sharply to normal. This fall in the temperature is very impressive, but certain questions immediately arise to the mind. Might not this be due to a simple antipyretic action exerted by the drug and, as such, perhaps not calculated to have a favourable influence on the outcome of the disease? That this response to M. & B. 693 is something different from a means of lowering the temperature is suggested by two factors. Firstly, in most cases this fall in temperature is maintained from the moment it starts and, although minor rises of temperature, of fractions of a degree, may occur, they do not appear to be of great significance. In the second place, nothing could be more impressive than the change which takes place in the patient's appearance, behaviour and general well-being. From a being gravely ill, obviously ravished by a powerful toxin, grievously distressed and in pain, he is transformed, as if by a miracle, to a state of relative tranquility, peace and

freedom from pain. When M. & B. 693 was first used, I can recall several patients whose appearance was such as to suggest that a fatal outcome was imminent in a matter of hours, and in whom this striking change was brought about. Those two factors, then, and in particular the latter constitute evidence which is not unconvincing that the action of M. & B. 693 is more than that of a simple antipyretic.

The sudden fall in temperature leads to yet another question. Could this be nothing more than the crisis which normally occurs in the majority of cases of pneumonia about the seventh day of the disease? Admittedly in those cases which did not come under treatment with M. & B. 693 till the fifth or sixth day of the illness, such an opinion might well be justified. That this is not the case is suggested by the fact that a similar effect is shown in cases treated with the drug within the first twenty-four hours of the onset of the disease, and also in cases treated on the second, third and fourth days of the illness. The suggestion becomes a conviction when case after case, with very few exceptions, responds to the drug by a fall in temperature accompanied by an incontestible change for the better in the patient's

condition. Furthermore, in the greater proportion of cases this improvement is maintained and the patient strides rapidly along the road to recovery.

It thus becomes evident that in M. & B. 693 we have a drug capable of exerting an influence directly on the purveyor of the toxin causing the illness - the pneumococcus. Regarding the mode of action of M. & B. 693, information has been detailed in a previous section (page 21).

Table 1 below shows the number of cases admitted on a given day of illness.-

Table 1.

Day of Illness.	Cases admitted.
1st Day	12
2nd Day	26
3rd Day	21
4th Day	19
After 4th Day	7

Table 1a.

Age	No. of Cases.
12-19	26
20-29	15
30-39	10
40-49	11
50-59	10
60-69	12
70 plus	1

In this series of eighty-five cases of all ages (see Table 1a) treated with M. & B. 693, 63 cases, or 74.1% showed this response of fall in temperature (Evans and Gaisford, 60% <sup>fall</sup> in 48 hours) along with general improvement, within twenty-four hours. Four

cases (4.7%) died. In the remaining thirteen, or 15.5%, the response was variable. Five cases (5.9%) did not respond till 48-72 hours. In some of these cases the temperature fell within twenty-four hours, only to rise again on a subsequent day. In others there was no satisfactory response. These cases will be examined in more detail at a later stage.

Whitby,<sup>9</sup> in his experimental work on pneumococcal infections in mice, found that M. & B. 693 gave protection against Types I, II and III and in Group IV against Types V, VII and VIII. It will now be of interest to observe what effect M. & B. 693 exerts on the different Types of Pneumococcus as they occur in man. It may be that here we shall find a reason for the variable response in 16.3% of the cases. Could it be that a particular type of Pneumococcus is resistant to the action of the drug? The question also arises as to whether or not M. & B. 693 has any effect on pneumonia caused by organisms other than the pneumococcus, e.g. the streptococcus.

The incidence of the various types of pneumococci and other organisms causing pneumonia in this series of eighty-five cases is shown below in Table 2.



Table 2.

Organism.	No. of Cases.
Pneumococcus Type I	7
" Type II	33
" Type III	7
" Group IV	16
Mixed Pneumococcal	5
Other Mixed Organisms	1
Streptococci	4
Untyped	12

The types of Group IV organisms which occurred are shown in Table 3.

Table 3.

Type	No. of Cases.
4	3
5	3
7	2
8	1
9	2
12	1
13	1
14	1
16	1
19	1

In pneumonia due to Type I infection there were seven cases in this series. In five of those there was the dramatic fall in temperature, along with general improvement, in twenty-four hours. The remaining two cases, K 2 and A 1, did not show this response till seventy-two hours after admission.

Table 4 shows the day of illness on which patients suffering from Type I pneumococcal infection were admitted to hospital.

Table 4.

Type I	
Day of admission	No. of Cases
1st day	1
2nd day	3
3rd day	2
4th day	-
After 4th day	1

Thirty-three of the eighty-five cases which came under observation were due to Type II pneumococcus. It is noteworthy in passing that in this area of South East Scotland the largest proportion of the cases was due to this type of pneumococcus. The day of illness on which patients were admitted is

shown in Table 5.

Table 5.

Type II.	
Day of Admission	No. of Cases
1st day	2
2nd day	11
3rd day	9
4th day	7
After 4th day	4

Of these thirty-three cases, three died and of the remainder only three failed to respond by the drop in temperature after treatment with M. & B. 693. In those three cases there was an initial fall in temperature, ~~33.5-34.5~~ but this was not maintained. In case K 9 there was a rise of temperature along with a recurrence of symptoms after twenty-four hours and this was not affected by further administration of M. & B. 693, the temperature falling by crisis on the fifth day after admission. In case A 8 the patient responded well to M. & B. 693, the temperature, pulse and respiration rate falling to normal within twenty-four hours. Four days later, however, there was a recrudescence of symptoms and signs of pneumonic consolidation became evident on the opposite side of

the chest in the right lower lobe. Administration of M. & B. 693 after this occurrence produced no effect. After a favourable response in case D 1, the temperature rose again on the sixth day and fell again twenty-four hours later and continued normal.

Seven cases of Type III pneumococcal infection occurred in the series. The day of their admission is shown in Table 6.

Table 6.

Type III.	
Day of admission	No. of Cases
1st day	-
2nd day	1
3rd day	1
4th day	3
After 4th day	2

Except one case, A 6, in which the temperature did not fall till an interval of forty-eight hours had passed from the initial administration of the drug, all the others responded in twenty-four hours. In one case, however, A 3, there was a recurrence of temperature which persisted for fourteen days in spite of continued treatment with M. & B. 693.

The series contained sixteen cases of infections

of the Group IV class, the various members of this class which occurred having already been shown in Table 2. The number of cases admitted on the various days of illness is shown in Table 7.

Table 7.

Group IV.	
Day of Illness	No. of Cases
1st day	4
2nd day	2
3rd day	5
4th day	5
After 4th day	-

In eleven of the cases the usual response to the drug was obtained. Two cases, G 9 and G 2, showed an irregular rise of temperature after the initial fall. In one patient, A 10, the drug had to be stopped and the temperature fell by lysis on the ninth day. Another, K 10, showed no response, the temperature falling on the eighth day, while in case L 2 the temperature rose twenty-four hours after the initial fall but subsided after a further forty-eight hours.

Pneumonia due to more than one organism occurred in four cases; the organisms were pneumococci as shown in Table 8.



Table 8.

Mixed Pneumococcal.	
Types of Pneumococcus	Case No.
Types 1, 16	D 7
Types 1, 18	E 14
Types 1, 6	B 15
Types 1, 6, 20, 22	B 18

Of the mixed pneumococcal infections only one responded in twenty-four hours to treatment with M. & B. 693. Two responded in forty-eight hours and one in seventy-two hours.

Four cases were due to the streptococcus and in those the temperature fell in twenty-four hours and remained normal. A fifth showed a mixture of haemolytic and non-haemolytic streptococci, staphylococci and micrococcus catarrhalis and failed to respond to M. & B. 693.

There were thirteen cases in which the causal organism was not determined. In only one of these, E 7, was there any subsequent rise in temperature after the initial fall. A 5 did not respond till seventy-two hours later and then remained normal.

In these preceding pages, then, we have summarised how the various types of pneumococci responded

to treatment with M. & B. 693. The question now arises why certain cases failed to respond. Can we throw any light on this matter? In the first place we must ask ourselves if in any of the cases which failed to respond in the normal manner there was inadequate dosage. In cases K 2 and A 7, both Type I, which did not respond till seventy-two hours after the beginning of treatment, the usual dosage of the drug was not given till this time had elapsed. Vomiting occurred in cases K 10 (Group IV) and A 10 (Group IV) and it is reasonable to assume that because of this the drug was not absorbed in sufficient quantity into the blood stream. In cases A 3 (Type III), D 1 and K 9 (Type II) and E 9 (untyped) the standard dose which in the majority of cases produced an adequate blood concentration was given but, in spite of showing an initial response, this was not maintained, temperature recurring at a later stage in all cases. Could it be that even with the normal dose those individuals were unable to maintain a sufficient blood concentration either through failure of absorption or too rapid excretion? The dosage in these cases was, A 3 - 21 grms., D 1 - 31 grms., K 9 - 40 grms., E 9 - 16 grms. Another explanation might be that a recrudescence of

the pneumonia process had occurred. This was certainly the case in case A 8 (Type II), in which signs of consolidation occurred in the other side of the chest. A striking feature about this new pneumococci process is that M. & B. 693 exerted no influence on it in spite of large dosage. Regarding this failure of M. & B. 693 to influence such a recrudescence, it is interesting to recall the observations of Telling and Oliver<sup>25</sup> who found that after treatment with M. & B. 693 the pneumococcus isolated from the sputum was atypical and did not give the agglutination reaction with the type specific serum as it had originally done. This raises the question as to whether in this case A 8 and in those others in which there was a recrudescence of symptoms after the initial fall, the rise in temperature might not be due to a low-grade infection with a changed type of pneumococcus. That such a changed organism might be resistant to M. & B. 693 is suggested by Whitby<sup>53</sup> (Bradshaw Lecture) who drew attention to the occurrence of resistant strains of organisms. He instanced cure in some acute cases of gonorrhoea, while in others the occurrence of a recrudescence of infection showed resistance to the compound. It may be asked if such a resistant

strain could develop in the short space of twenty-four hours to six days and, in answer to this, it may be said that Telling and Oliver<sup>25</sup> found these changed pneumococci after administration of 3 grms. M. & B. 693.

In two cases, G 9 and G 2 (Group IV) the recurrence of temperature might be said to be due to the presence of fluid at the lung base. After removal of this, the symptoms subsided.

Only one case of mixed infection responded to M. & B. 693. In one, D 7, there was complete lack of response in spite of a dosage of 21 grms. In the remaining two cases, B 15 and B 18, a dosage of 13 grms. and 15 grms. respectively was necessary before the temperature fell to normal. It is perhaps not unreasonable to suppose that these cases are more resistant to treatment and that their response to M. & B. 693 will be variable.

In spite of the fact that the response of certain cases in this series has been variable, it seems that the only group in which we must say the action of M. & B. 693 is doubtful is that in which mixed infections occur. I say this because, out of four cases, in one the drug failed completely and in two others a

larger dosage was required. In all other types the majority of cases responded and in those which did not there had been the possibility of too little of the drug, through vomiting, entering the blood stream or, in other cases, recrudescence, possibly due to a resistant or changed organism. It seems certain, then, that when a diagnosis of pneumonia is made on clinical grounds, M. & B. 693 should be employed and, if this is done, there is every reason to expect a favourable response. The procedure of typing sputum is thus unnecessary.

Perhaps one of the first questions asked when a new preparation appears for the treatment of a disease is what effect does it have on the mortality. Such a question is natural in the case of all diseases but in none more so than pneumonia, for very often it is responsible for a large number of deaths in people who are in the prime of life.

Of the eighty-five cases, at no matter what stage of the disease M. & B. 693 was given, only four died, giving a mortality of 4.7%. In the absence of a control series, a strict comparison cannot be made but a figure such as this in a group of cases of different types of lobar pneumonia is far below any recorded with other methods of treatment, even taking



into account the well-known variation in the severity of the disease.

Table 9, below, shows the mortality from all cases of lobar pneumonia admitted to the Royal Infirmary, Edinburgh, over the preceding five years.

Table 9.

Year	1933- 1934	1934- 1935	1935- 1936	1936- 1937	1937- 1938
Mortality	23.28%	28.4%	41.66%	49.2%	39.22%

In seven cases of Type I there were no deaths. Out of sixteen cases of this type Graham et al<sup>28</sup> had no deaths, and Flippin et al<sup>27</sup> in twenty-six cases report similar findings. Pepper<sup>54</sup> et al, on the other hand, in one hundred and four cases of Type I pneumonia had a mortality of 5.8%.

Type II pneumococcus was responsible for three of the four deaths in this series - Cases A 7, B 14, K 8. All of these patients were over forty years of age. Case A 7 responded well to the drug, the temperature falling within twenty-four hours. The temperature remained normal but on the fifth day the patient died and at post-mortem examination, double pneumonia,

hypertrophy and dilatation of the heart along with an old-standing pericarditis, were found. Case B 14 had marked pleural bronchitis and died shortly after admission. Case K 8 was an old man whose temperature was never high but in whom there were undeniable signs of pulmonary consolidation confirmed by X-ray examination. Large doses of M. & B. 693 failed to prevent the fatal outcome.

These three deaths constitute a mortality of 9.6% from this type. Pepper et al<sup>54</sup> had thirty cases of Type II infection in their series of four hundred cases, with a mortality of 6.7%. No deaths occurred in the four cases occurring in the series reported by Graham et al<sup>28</sup>.

In pneumonia caused by Type III, of which there were seven cases, all survived. This type of pneumococcus is well known for the frequency with which it attacks people over forty years old and for its all too frequently fatal outcome. Even in a small number of cases the failure of Type III pneumococcus to cause any deaths is encouraging. In four hundred cases, Pepper et al<sup>54</sup> had sixty-three cases, with a mortality of 16.4%.

No deaths occurred in pneumonia due to Group IV mixed or streptococcal infections. The remaining

death was case L 6, in whose sputum no pneumococci were found. This case was complicated by the presence of carcinoma of the oesophagus and it is of no little interest to note that after treatment with M. & B. 693 his temperature returned to normal. Several days later, however, he succumbed to the original disease.

This very striking reduction in the mortality from pneumonia with the use of M. & B. 693 is extremely gratifying and in itself is a strong argument in favour of the use of the drug.

With a drug such as M. & B. 693 it is important that we should reach some conclusion about dosage and as to the best method of employing the preparation. From animal experiments with M. & B. 693 it soon became evident that with a given dosage certain variations of the concentration of the drug in the blood stream occurred. Baines and Wien<sup>18</sup>, Bliss and Long<sup>55</sup>, and Hobson and MacQuaide<sup>21</sup> showed that in man such was also the case. The variations in blood concentration experienced are thought to depend on such factors as the rate of absorption, rate of excretion and rate of acetylation of the drug, (Stokinger<sup>19</sup>). That the general state of health may also play a part is postulated by

Hobson and McQuaide<sup>21</sup>. In view of this, then, one wondered if it might be necessary to estimate the blood concentration of the drug by elaborate laboratory means throughout a course of treatment. Should this prove to be the case, the scope of the drug must then be limited to places in which such investigations could be made.

Flippin et al<sup>27</sup> were able to show, however, that a concentration of 1 to 2.8 mgm. per 100 cc.s was as effective as a concentration of 10 mgms. or more per 100 cc.s. The important practical consideration, then, was to know if a stated dosage would, in a sufficiently large number of cases, produce a concentration in the blood stream which would be adequate to overcome the pneumococcus.

Evans and Gaisford<sup>11</sup> in their original series gave one tablet, or 0.5 gm. four-hourly for the first three or four days, followed by one tablet twice daily for two to three days, giving in all a total of 12 gms. In the absence of severe toxic symptoms they later suggested that the dose should be increased, to 2 gms. - four tablets on admission followed by 1 gm. - two tablets, four-hourly for seventy-two hours, making a total of 25 gms. - fifty tablets. In this series,

as stated before, the practice has been to give a uniform dose in most cases in the first twenty-four hours, as follows:- Four tablets, 2 gms., on admission, followed by a similar dose four hours later and then 1 gm., two tablets, four-hourly for four doses. After this the subsequent dosage was varied and will be dealt with later. By this means a dosage of 7-8 gms., fourteen to sixteen tablets, was given in the first twenty-four hours. In a large proportion of cases this dosage was sufficient to produce a response as shown by fall in temperature and general improvement in twenty-four to thirty-six hours. It is thus reasonable to deduce that this dosage is sufficient to produce a concentration in the blood adequate to overcome the pneumococcus. That this dosage is necessary is borne out by the fact that in cases where this amount was given over a longer period, no response occurred till it had been given in full.

This point can best be illustrated by the following cases, viz:- Case C 4, 14 tablets or 7 gms. M. & B. 693 were given over a period of thirty-two hours and then the response was obtained. In case K 2, 14 tablets or 7 gms. M. & B. 693 were given in seventy-two hours and in case A 1, 15 tablets or  $7\frac{1}{2}$  gms. in



the same period and it was only at the end of this time that the temperature fell to normal.

This point is illustrated in Table 10 below.

Table 10.

Case No.	C 4	K 2	A 1
Dose M. & B. 693	7 gms.	7 gms.	7 gms.
Time in which given	32 hrs.	72 hrs.	72 hrs.
Time taken for response	32 hrs.	72 hrs.	72 hrs.

It thus becomes obvious that the sooner adequate dosage is administered the sooner a favourable response may be expected.

With regard to the total dose of M. & B. 693, this was varied within certain limits throughout the series. The results are drawn up in tabular form in Tables 11 (a) and (b), Table 12, Table 13 (a) and (b), Table 14 and Tables 15 (a) and (b).

Table 11 (a).

M. &amp; B. Total Dose - 18-26 Tablets.

Case No.	K 5	C 9	M 4	C 8	C 11	M 1	C 12	H 16	B 17
Response	+	+	+	+	+	+	+	+	+
Remarks	Nil	Vomit	Vomit	Nausea	Vomit	Aet 13	Nil	Nil	Aet 14

Table 11 (b).

18-26 Tablets.

Case No.	C 6	E 4	M 3	K 1	F 6	B 16	B 12
Response	+	+	+	+	+	+	+
Remarks	Death	Nil	Aet 81	Nil	Nil	Nil	Pregnant

Table 12.

27-30 Tablets.

Case	C 4	H 12	A 10	C 5	A 7	A 4	A 11	E 18	A 5	A 2	D 2	D 9
Response	+	+	-	+	+	+	+	+	+	+	+	+
Remarks	Nil	Aet 15	Severe Vomit	Aet 14	Nil	Nil	Nil	Nil	72 hrs.	Nil	Nil	

Table 13 (a).

31-36 Tablets.

Case No.	F 2	E 12	E 8	D 6	D 4	C 7	B 19	M 2	D 5	D 8
Response	+	+	+	+	+	+	+	+	+	+
Remarks	Nil	Nil	Nil	Nil	Nil	Nil	Later Empy.	-	Temp 11th day	Nil

Table 13 (b).  
31-36 Tablets.

Case No.	D 3	A 6	C 3	E 5	G 1	A 9	A 8	E 13	E 7	D 10	E 11
Response	+	+	+	+	+	+	+ -	+	+	+	-
Remarks	Nil	Nil	Nil	Nil	Nil	Nil	Other side	Nil	Temp. after 3 days lasted 5	Nil	

Table 14.  
37-50 Tablets.

Case No.	L 2	L 3	L 1	L 4	E 6	K 9	H 13	D 7	F 1	A 3	B 13	K 2	G 3
Response	+ -	+	+	+	+	+	+	-	+	-	+	+	+
Remarks	Temp. 48 hrs.	Nil	Nil	Nil	Nil	Nil	Nil	No Re- sponse		Temp. for 14 days			

Table 15 (a).  
50 Tablets or more.

Case No.	K 3	K 6	K 7	K 8	K 11	H 10	H 15	D 1	K 4	K 10	G 2
Response	+	+	+ -		+	+	+	+ -	+	-	+ -
Remarks	Very ill		Temp. for 7 days after fall			Severe temp. Empy.		Temp. 6th day remain up		Temp. fell 8th day	Fluid

Table 15 (b).  
50 Tablets or more.

Case No.	G 9	G 7	H 11	B 18	E 10	G 8	H 14	G 6
Response	+ -	+ -	+	+ -	-	+	+	+
Remarks	Fluid	Axillary Adenitis		Temp. 6th day	No Re- sponse			

In the cases in which the total dosage did not exceed 26 tablets, or 13 grms., there was usually some reason such as vomiting for stopping the drug at this stage. It is significant to note that all these cases made an uneventful recovery.

Where the total dosage was 27 to 30 tablets -  $13\frac{1}{2}$  to 15 grms. - only one case failed to respond and here again there was severe vomiting. Once again these cases made a good recovery.

When the final dose was not more than 36 tablets - 18 grms. - the immediate response was for the most part good. In five cases, however, the convalescence was interrupted by further rises in temperature which were not completely influenced by the drug.

In those cases in which a total of from 15 to 25 grms. of M. & B. 693 was given, two failed to respond and had continued temperature uninfluenced by the drug.

Another responded but the temperature rose forty-eight hours later and again fell with M. & B. 693.

A dosage in excess of 25 grms. - 50 tablets - was given in nineteen cases. In ten of these the only reason for so doing was to assess the end effects. In so far as the immediate response and subsequent convalescence were concerned, there was nothing to note. In the remaining nine the drug was continued because of complications which are shown in the Tables 15 (a) and (b).

My experience with M. & B. 693 leads me to believe that the drug exerts its influence mainly on the early stages of the disease, and for this reason I believe that a dosage of 7-8 grms. - 14-16 tablets - should be given in the first twenty-four hours after seeing patients. From the foregoing Tables it can be seen that the larger subsequent doses do not appear to prevent the onset of complicating factors, and furthermore, once these factors have arisen it seems doubtful if M. & B. 693 is capable of influencing them. Cases with uninterrupted convalescence occurred in the group on the smallest total dosage and on the largest. Where complications occurred, larger doses were given but seemingly with little benefit. In view of this,



I do not consider that large subsequent doses are necessary. A total dosage of 14-18 grms. - 28-36 tablets - should be sufficient in most cases.

There is just one point about those complicating factors, such as a relighting of the pneumonic process. It seems that this illness is not so acute as it might otherwise have been.

The actual effect of M. & B. 693 on the pneumonic process in the lung is difficult to assess. On this point I agree with Pepper, Flippin and Schwartz<sup>54</sup> that once red hepatization has occurred, M. & B. 693 does not influence the process. It would appear that the changes in the lung progress as previously. In the normal course of events the lungs should have returned to normal within fourteen days (Price<sup>17</sup>), and this is the case in a great number of the present series. A certain proportion, however, showed delay in this process - E 10, E 11, H 15, D 5, D 3, M 2, C 7, C 9, G 2, G 7 - i.e. 11.63%.

Seven of these cases were X-rayed during convalescence and the results are tabulated in Table 16.

Table 16.

No. of Case.	X-ray Reports.	Day after admission.
M 2	Almost complete resolution	43 days
C 7	Resolving Pneumonia	24 days
E 11	Unresolved	37 days
H 15	Still some obscurity	49 days
C 9	Delayed resolution of Inflammatory Process	45 days
G 2	Unresolved	15 days
G 7	Consolidation right base	15 days

Considerable delay in resolution has thus appeared in some cases. It is of interest to note the dosage of M. & B. 693 that those patients received. This is shown in Table 17 below.

It does not appear that the dosage of the drug bears any relationship to the prevention of delay in resolution, as this has occurred with as small a dose as 8 grms. - 16 tablets - and as large a dose as 33 grms. - 66 tablets.

Table 17.

Case No.	Dose of M. & B. 693				
M 2	17	grms.	or	34	tabs.
C 7	18	"	"	36	"
E 11	18	"	"	36	"
H 15	34	"	"	68	"
C 9	8	"	"	16	"
G 2	22	"	"	44	"
G 7	32 $\frac{1}{2}$	"	"	65	"
E 10	26	"	"	52	"
D 5	17	"	"	34	"
D 3	16 $\frac{1}{2}$	"	"	33	"

A non-purulent pleural effusion occurred in two cases - G 9 and G 2 - causing an irregular rise in temperature. Aspiration of the fluid brought about complete recovery.

Empyema was present in two cases - H 10 and B 19. Both were due to Type II pneumococcus. Case B 19 was discharged to a convalescent home twenty days after admission, the temperature, etc., being normal. Eighteen days later, however, he showed signs of an inter-lobar pneumonia which had to be treated surgically. H 10 also required surgical drainage. M. & B. 693 is known to be present in purulent pleural exudates in a concentration of  $\frac{1}{3}$  to  $\frac{2}{3}$  that of the blood concentration, and the possibility of treating empyema by repeated aspiration and continuation of the drug

has been suggested. In view of the fact that despite large doses of M. & B. 693 (H 16 had 36 grms.), complications such as empyaema still occur, I do not feel that such treatment would be justified at this stage.

The incidence of empyaema during the preceding five years, in the Royal Infirmary, Edinburgh, is shown in Table 18.

Table 18.

Year	1933 1934	1934 1935	1935 1936	1936 1937	1937 1938
No. of Cases	3.7%	4.3%	0.33%	10.3%	0.55%

From these figures it is not possible to give any definite opinion as to whether or not the incidence of empyaema in cases treated with M. & B. 693 is less than previously. It seems justifiable to say, however, that it is not higher than the average figure of the last five years. In seventy cases Smith and Needles<sup>56</sup> had only one case of empyaema. Similarly, in one hundred cases Flippin et al<sup>27</sup> had none. In contrast to those we have Evans and Gaisford's<sup>11</sup> figure of six cases of empyaema in sixty cases treated with the drug.

The toxicity of M. & B. 693 for man was judged to be low by Evans and Gaisford<sup>11</sup> in their original investigation. My findings agree with theirs in that I found the main toxic symptoms to be cyanosis and vomiting. These proved to be more troublesome than dangerous.

Cyanosis occurred in 8.1% of the patients in a varying degree, but in none was it considered necessary to discontinue the drug, and at the end of treatment the methaemoglobinuria cleared rapidly.

Nausea and vomiting were encountered in 15% of the cases. In only four - A 10, C 9, D 1, C 11 - was it found necessary to stop the administration of the drug.

A 10 had severe vomiting after she had received twenty-eight tablets in two days. The drug was discontinued and the temperature fell by lysis on the ninth day.

D 1 had twenty-two tablets before vomiting and the temperature had fallen less than twelve hours after admission. The drug was discontinued but the temperature rose again on the sixth day, when the drug was recommenced in spite of a tendency to vomit.

C 11 received in all twenty-three tablets before



the drug had to be stopped because of vomiting. The temperature fell after fourteen tablets, and remained normal.

C 9 had sixteen tablets before vomiting made it necessary to discontinue the drug. Flippin et al<sup>27</sup> had vomiting in 40% of their one hundred cases.

Where vomiting was threatened, certain measures were instituted to attempt to overcome this, viz. the tablets were crushed and given in milk, or a mixture of sodium bicarbonate (30 grains) was given with the drug, with satisfying results. Flippin et al<sup>27</sup> believe that a mixture of sodium chloride and dextrose, given intravenously, is the best method of combating vomiting.

Toxic symptoms of a much more severe character have been reported, but fortunately they are the exception rather than the rule. In one hundred cases, Flippin et al<sup>27</sup> had a case in which the white blood count was reduced to 1800. Graham et al<sup>28</sup> report a case of granulocytopenia after 79 grms. (158 tablets) M. & B. 693, with recovery, and Barnett et al<sup>34</sup> report the death of a child aged ten after 80.9 grms. (161 tablets) M. & B. 693 in seventeen days. These two latter cases were both given very high dosages of the

drug. All cases in this series had white blood counts made on admission, most of them after an interval of from three to five days, and a considerable number towards the tenth day after admission. In none was there a fall of the white cell count to a level lower than that which would normally be found as the condition improved. Blood films were not made so no opinion can be given as to whether the drug was responsible for any alteration in the characters of members of the white series.

A point of some interest in treatment of pneumonia with M. & B. 693 was to endeavour to determine if there was any shortening of the duration of stay in hospital. This is a matter of no small importance when one considers the demand for beds in our general hospitals, and also the added expense of maintenance that each day of stay therein means. In uncomplicated cases the average duration of stay of each patient was 18.6 days. This compares very favourably with the duration of stay in previous years. A comparison is shown in Table 19 below.

Table 19.

Year	1933 1934	1934 1935	1935 1936	1936 1937	1937 1938	M & B 693
Duration of stay Uncomp. cases	28.1 days	26.1 days	25 days	25 days	22.6 days	18.6

It is not yet possible to give an opinion on whether there is any shortening of the period of convalescence or not. It is perhaps not too much to hope that when the patient is spared the strain and absorption of toxins of the early days of the disease that his period of recovery may be shortened.

A matter of great importance is the cost of such a drug. Is it within the reach of all pockets or is it such that it can only be obtained by the richer members of society or in hospital? It has the advantage of being relatively cheap. For 50 tablets, or 25 grms., which is the maximum dosage required in most cases, the cost is in the region of twelve shillings. Not only has M. & B. 693 the advantage of being relatively cheap itself, but its use makes the employment of other expensive material previously necessary in pneumonia, e.g. oxygen, seldom necessary or, if needed, then for a much shorter time.

M. & B. 693 has therefore shown itself to be a definite advance in the fight against pneumonia, being universally applicable, simple in use, relatively free from toxic symptoms which, as a rule, are not serious, and comparatively cheap. Also it acts in the majority of cases of clinically diagnosed pneumonia and there

are no apparent contra-indications to its use.

We have, then, a drug which can be used by the General Practitioner of Medicine in the treatment of pneumonia. Having made the clinical diagnosis of pneumonia there is no need for him to have the sputum typed. He can straightway employ the compound without fear of serious toxic symptoms, with the anxious seven days to the crisis removed, and with reasonable certainty of a favourable outcome for his patient.

S U M M A R Y.

1. Eighty-five cases of pneumonia have been treated with 2-sulphanilyl amino pyridine M. & B. 693.
2. 74.1% of the cases responded to treatment with M. & B. 693 in 24-36 hours, e.g.-
  - (a) A dramatic sharp fall in temperature, pulse and respiration rate to normal;
  - (b) A striking improvement in the general well being of the patient.
- 5.8% of the cases showed the same response in 48-72 hours.
- 15.5% of the cases showed a variable response.
3. M. & B. 693 exerted an action on pneumonia caused by Types I, II, III and the members of Group IV pneumococcus.
4. M. & B. 693 exerted an action on pneumonia caused by the streptococcus.
5. M. & B. 693 was indefinite and unreliable in its action on pneumonia due to mixed pneumococcal or other mixed infections.
6. The action of M. & B. 693 occurred irrespective of the day of the disease.
7. M. & B. 693 was effective in pneumonia in all the age groups in this series.



8. Four cases in this series died - a mortality of 4.7%. This death-rate is compared with that occurring for the past five years in the Royal Infirmary, Edinburgh.
9. Favourable results from M. & B. 693 are dependent on an adequate dose when drug is first given.
10. A dose of 7-8 grms - 14-16 tablets - should be given in the first 24 hours of administration.
11. Providing a dose of 7-8 grms is given in the first 24 hours of administration, subsequent dosage is not so important, the outcome being as good in cases on low total dosage as high.
12. M. & B. 693 does not influence the pneumonic process in the lungs.
13. 11.6% of cases in the series showed delayed resolution.
14. Delay in resolution does not appear to be influenced by total dosage of M. & B. 693, cures occurring with low and high total doses.
15. Empyema occurred in two cases.
16. No severe toxic symptoms occurred.  
  
Vomiting was present in 15% of cases; in four cases the drug had to be stopped.  
  
Cyanosis was present in 8.1% of cases.  
  
There was no adverse effect on the white blood cells.

17. Duration of stay in hospital in uncomplicated cases was 18.6 days. This is compared with the stay in previous years.
  18. No conclusion is possible as to any change in the length of convalescent period.
  19. The cost of the drug is within the reach of most people.
  20. M. & B. 693 is a definite advance in the therapy of pneumonia.
  21. M. & B. 693 can be used with safety and reasonable hope of certainty by the General Practitioner of Medicine.
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